DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Dedicated

to

my Family,

friends

&

Teachers

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Dr. Karanpreet Singh

ABBREVIATIONS

AF	Atrial Fibrillation
AV	Atrio-ventricular
BMI	Body Mass Index
BNP	Brain natriuretic peptide
CAD	Coronary artery disease
CBC	Complete blood count
CHARM	Candesartan in heart failure assessment of reduction in mortality and morbidity
CI	Class interval
CKD	Chronic kidney disease
CLD	Chronic liver disease
COPD	Chronic obstructive pulmonary disease
DD	Diastolic dysfunction
DMCH	Dayanand medical college and hospital
DBP	Diastolic blood pressure
DST	Diastolic stress test
E/A	Peak velocity blood flow from LV relaxation in early diastole / Peak velocity blood flow in late diastole caused by atrial contraction
E/e’	Peak velocity blood flow from LV relaxation in early diastole / Mitral annular velocity in early diastole
ECG	Electrocardiography
EF	Ejection fraction
GLS	Global longitudinal strain
Hb	Hemoglobin
HDL	High density lipoprotein
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HTN	Hypertension
HR	Heart rate

LAVi	Left atrium volume index
LBBB	Left bundle branch block
LDL	Low density lipoprotein
LFT	Liver function tests
LV	Left ventricle
LVEF	Left ventricle ejection fraction
LVFP	Left ventricle filling pressure
LVH	Left ventricle hypertrophy
NT-pro BNP	N-terminal pro brain natriuretic peptide
OPD	Outpatient department
OR	Odds ratio
PASP	Pulmonary artery systolic pressure
RBBB	Right bundle branch block
RBS	Random blood sugar
RFT	Renal function tests
RWMA	Regional wall motion abnormalities
SBP	Systolic blood pressure
SD	Standard deviation
SPECT	Single photon emission computed tomography
SPO2	Peripheral capillary oxygen saturation
SR	Sinus rhythm
TG	Triglycerides
TLC	Total leucocyte count
TMT	Treadmill test
TR	Tricuspid regurgitation
VO2	Oxygen consumption
2-D	2-dimensional

ABSTRACT

Introduction: Heart failure with preserved ejection fraction (HFpEF) accounts for approximately 50% of HF cases and its prevelance relative to HF with reduced EF is rising.[1] Diastolic stress test echocardiography can offer higher sensitivity over echocardiography at rest for diagnosis of HFpEF in early stages.

Aim: To study the importance of diastolic stress test echocardiography in diagnosing cases of HFpEF in early stages, when echocardiography at rest is normal.

Methods: A hospital based observational study involving 150 cases in OPD of DMCH. The cases are divided into 2 groups. Group A contains 75 cases of suspected HFpEF and group B contains 75 cases of asymptomatic hypertension. Only cases with a normal echo at rest were included. Diastolic stress test (DST) echocardiography was done after TMT to determine the proportion of cases in each group which develop overt HFpEF during DST echo.

Results: In group A, mean age was 54.11±11.6 years and 65% were males. Out of 75 cases in this group, 42 had abnormal DST echocardiography which accounted to 56% of cases. The patients with abnormal DST echocardiography were predominantly diabetic (73.8% vs 18.2%; p-value = 0.001), smoker (38.1% vs 6.1%; p-value =0.0001), had a higher BMI (24.42±3.19 vs 22.44±3.22 kg/m^2; p-value =0.010) and higher BNP levels (142.24±37.79 vs 81.12±23.64 pg/ml; p-value =0.000). On multivariate logistic regression analysis, diabetes mellitus was found to be the independent predictor of abnormal DST echocardiography (OR=8.81, CI= 2.595- 29.902; p-value =0.000).

In group B, mean age was 61.01±8.14 years with 65.3% males. 2 out of 75 cases tested HFpEF+ on stress, which amounts to only 2.7% of the total cases.

Conclusion: The findings in this study suggest that DST echocardiography using E/e' ratio can have a significant role in cases of suspected HFpEF in early diagnosis and diabetes mellitus was found to be the independent predictor of abnormal DST echocardiography in these cases. In asymptomatic cases, even in the presence of hypertension which is an important risk factor for HFpEF, DST echocardiography has a very limited role.

Keywords: HFpEF, echocardiography, DST echocardiography, BNP.

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INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) accounts for approximately 50% of HF cases and its prevelance relative to HF with reduced EF is rising[1]. Hypertension in particular is a strong risk factor; 80 to 90 percent of the patients of HFpEF are hypertensive.[2] In the general population aged >=60 years, 4.9% were identified to have heart failure with preserved ejection fraction (HFpEF), implying that there could be several millions of affected individuals, most of whom remain undiagnosed with conventional echocardiography.[3]

The diagnosis of heart failure with preserved ejection fraction (HFpEF) remains on the basis of echocardiography at rest. However, some patients with HFpEF have symptoms such as dyspnea only during exertion. Accordingly, non-invasive echocardiographic analysis at rest could be less sensitive to identify these patients. In line, recent studies demonstrated that in some patients with HFpEF left ventricular diastolic abnormalities occur only during exercise.[4] Heart failure with preserved ejection fraction (HFpEF) is an emerging global health problem of which there is limited awareness.[5] HFpEF has a prognosis similar to that of heart failure with reduced ejection fraction (HFrEF) and accounts for approximately half of all patients with heart failure.[5] Risk factors include older age, female sex, obesity, hypertension, tobacco use, diabetes mellitus, coronary artery disease (CAD), valvular heart disease and atrial fibrillation.[6] Heart failure with preserved ejection fraction typically evolves from a combination of risk factors and comorbidities, including advanced age, female sex, obesity, systemic arterial hypertension, diabetes mellitus, renal dysfunction, anemia, iron deficiency, sleep disorders, and chronic obstructive pulmonary disease[7-12]. Basic mechanisms affecting the myocardium in HFpEF include myocyte hypertrophy, systolic and diastolic dysfunction, energetic abnormalities, interstitial fibrosis, inflammation, increased oxidative stress, endothelial dysfunction, and impaired density and autoregulation of the microcirculation.[13,14]

With the increase of incidence of non-communicable diseases such as diabetes mellitus, hypertension, obesity and with changing lifestyles, the incidence of HFpEF is increasing.[3] There is a need to diagnose HFpEF at an early stage so that aggressive intervention can be pursued as early in the course of the disease as possible. In general, BNP levels are higher in patients presenting with acute shortness of breath for cardiac reason or in acute HF, than in patients who have chronic HF.[15,16]. Natriuretic peptide levels can be normal in these patients even with invasively confirmed HFpEF. In consequence, normal BNP levels do not exclude HFpEF, especially in the presence of obesity.[17] Interpretation depends also on whether the patient is in sinus rhythm (SR) or has atrial fibrillation (AF), which itself is associated with increased NP levels even in the absence of HF.[18,19]

Left ventricular (LV) diastolic dysfunction should be suspected in patients with known or suspected heart failure (eg, patients with possible cardiogenic dyspnea) as well as in asymptomatic patients with hypertension.[20] LV diastolic dysfunction can cause symptoms of dyspnea and reduced exercise tolerance in patients with heart failure with reduced ejection fraction and heart failure with preserved ejection fraction. Thus, assessment of diastolic function is an integral component of the echocardiographic examination in patients referred with a diagnosis of dyspnea or heart failure. Evaluation of diastolic function in asymptomatic patients with hypertension is also reasonable, as echocardiographic findings of diastolic dysfunction and its progression or lack thereof have been shown to predict clinical events of death and heart failure in observational and community studies. [20]

Diastolic dysfunction or HFpEF occurs when the left ventricular myocardium is non-compliant and not able to accept blood return in a normal fashion from the left atrium. [21] This can be a normal physiologic change with aging of the heart or result in elevated left atrial pressures

leading to the clinical manifestations of diastolic congestive heart failure. There are four grades of diastolic dysfunction:

1. Grade 1 (impaired relaxation) with normal E/e' ratio and E/A<1.
2. Grade 2 (pseudonormal) with elevated E/e' ratio and E/A 0.8 +- 1.5 and E/A<1 on performing valsalva.
3. Grade 3 (reversible restrictive) with elevated E/e' ratio and E/A>2 and E/A<1 on performing valsalva.
4. Grade 4 (fixed restrictive) with elevated E/e' ratio and E/A>2 and lack of E/A reversal on valsalva.

Echocardiography is the gold standard to diagnose overt diastolic dysfunction.[21]. However, standard 2-D echocardiography is insufficient in diagnosing cases of HFpEF in early stages as such patients develop symptoms only during stress. There is a need for better understanding of diastolic stress test echocardiography and the advantages it offers in diagnosing early cases of HFpEF, where standard echocardiography at rest has very low sensitivity. Stress echocardiography can also show the odds of having coronary artery disease, diagnose significant blockages in the arteries; and tell the effectiveness of a person's cardiac treatment plan[22].

Early in the course of the disease when a patient develops symptoms of heart failure only during exertion, a patient will have normal echocardiographic findings at rest and will have BNP with normal range. This is the reason why HFpEF goes undiagnosed in most cases until further down the course of the disease until the patient develops symptoms at rest. In view of rising incidence of HFpEF and a very limited number of studies done on diastolic stress test echocardiography in suspected cases of HFpEF, more exploration in this field is needed so that cases of HFpEF can be detected at an early stage and early intervention can be started in order to stop or decrease the progression of the disease. If HFpEF occurs in a person, the earlier detection and treatment can lead to decrease in incidence of complications and death. Early detection of

HFpEF is just as important as the treatment itself. Early detection of HFpEF among people who are suspected to have HFpEF and among people who are hypertensives but are asymptomatic is main task to reduce morbidity and mortality. Exercise stress testing like dobutamine stress echocardiography, treadmill test and stress SPECT are routinely used for the non invasive assessment of coronary artery disease and is considered a safe procedure. These methods are not as commonly used for detecting HFpEF. In this study, treadmill test echocardiography method was used to detect HFpEF by measuring septal E/e' ratio. The E/e' ratio correlates with LV stiffness and fibrosis.[23]

AIM OF STUDY

The purpose of this study is to assess the potential usefulness of DST echocardiography in patients with HFpEF in early stages in 2 separate groups of patients- patients with suspected HFpEF and asymptomatic patients with arterial hypertension.

REVIEW OF LITERATURE

According to Gazewood JD et al[6], heart failure with preserved ejection fraction (HFpEF), also referred to as diastolic heart failure, is characterized by signs and symptoms of heart failure and a left ventricular ejection fraction (LVEF) greater than 50%.[6] Diastolic heart failure currently accounts for more than 50% of all heart failure patients.[24] The pathogenesis of diastolic dysfunction involves abnormalities of active ventricular relaxation and passive ventricular compliance, which lead to ventricular stiffness and higher diastolic pressures. These pressures are transmitted through atrial and pulmonary venous systems, reducing lung compliance. A combination of decreased lung compliance and cardiac output leads to symptoms.[6] Diastolic dysfunction by echocardiography is one of the criteria for the diagnosis of heart failure with preserved ejection fraction (HFpEF).[24]

A diagnosis of primary diastolic heart failure requires three obligatory conditions to be simultaneously satisfied: (1) presence of signs or symptoms of congestive heart failure; (2) presence of normal or only mildly abnormal left ventricular systolic function; (3) evidence of abnormal left ventricular relaxation, filling, diastolic distensibility or diastolic stiffness.[25]

A patient of suspected HFpEF is defined as having left ventricular ejection fraction >=50%, exertional dyspnoea, septal E/e' at rest 9–14, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) at rest <220 pg/mL[26]. HFpEF during stress is defined as E/e'>14 and LAVi>34ml/m^2. In a study conducted by Belyavskiy E et al[26], patients with suspected HFpEF (left ventricular ejection fraction 50%, exertional dyspnoea, septal E/e' at rest 9–14, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) at rest <220 pg/mL; n = 13) and a control group constituted from asymptomatic patients with arterial hypertension (n = 19) and healthy subjects (n = 18) were included. All patients were analysed by two-dimensional and Doppler echocardiography at rest and during exercise (DST) and underwent

cardiopulmonary exercise testing and NT-proBNP analysis during exercise. HFpEF during exercise was defined as exertional dyspnoea and peak VO2 <=20.0 mL/min/kg. In patients with suspected HFpEF at rest, 84.6% of these patients developed HFpEF during exercise, whereas in the group of asymptomatic patients with hypertension and healthy subjects, the rate of developed HFpEF during exercise was 0%. Regarding the diagnostic performance of DST to detect HFpEF during exercise, an E/e' ratio >15 during exercise was the most accurate parameter to detect HFpEF (accuracy 86%), albeit a low sensitivity (45.5%). Nonetheless, combining E/e' with tricuspid regurgitation (TR) velocity >2.8 m/s during exercise provided a significant increase in the sensitivity to detect patients with HFpEF during exercise (sensitivity 72.7%, specificity 79.5%, and accuracy 78%). Consistent with these findings, an increase of E/e' was significantly linked to worse peak VO2, and the combination of an increase of both E/e' and TR velocity was associated with elevated NT-proBNP values during exercise.

According to Popescu BA et al[27], assessment of LV function during exercise or stress seems to be intuitive in HFpEF patients as their symptoms occur mainly with exertion. Patients with HFpEF have limitations in increasing their LV stroke work to meet the metabolic demand at exercise due to dynamic impairment of LV active relaxation and contraction. An increase of LVFP with exertion is needed to maintain adequate LV filling and stroke volume. Recent studies have shown a variety of abnormalities of systolic and diastolic function on exercise in patients with HFpEF: reduced myocardial systolic strain, reduced ventricular systolic apical rotation at rest (which fails to increase normally on exercise), reduced mitral annular motion in systole and diastole and delayed ventricular untwisting associated with reduced LV suction.

Heart failure with preserved ejection fraction typically evolves from a combination of risk factors and comorbidities, including advanced age, female sex, obesity, systemic arterial hypertension, diabetes mellitus,

renal dysfunction, anaemia, iron deficiency, sleep disorders, and chronic obstructive pulmonary disease.[28]

According to Gutierrez C et al[29], chronic hypertension is the most common cause of diastolic dysfunction and failure. It leads to left ventricular hypertrophy and increased connective tissue content, both of which decrease cardiac compliance. The hypertrophied ventricle has a steeper diastolic pressure-volume relationship; therefore, a small increase in left ventricular end-diastolic volume (which can occur with exercise, for example) causes a marked increase in left ventricular end diastolic pressure.

Gibby C et al[30] states that most measures that use E/e' to characterize LV function are obtained at rest. While overt LV diastolic and systolic dysfunction can be readily identified by conventional diagnostic techniques including echocardiography, the initial stages of myocardial dysfunction may be hidden by compensatory mechanisms, especially at rest. In patients with a similar grade of DD at rest, there can be a spectrum of alterations in diastolic function during exercise.

The evaluation of left ventricular diastolic function at rest is an integral part of echocardiography. If first degree of diastolic dysfunction is found in the resting examination, or if there is a large clinical suspicion of heart failure and the previous examination does not give us the final diagnosis, it is worth to refer the patient to the echocardiographic diastolic stress test.[31]

Traditional models of HFpEF pathophysiology revolve around systemic HTN and other causes of increased left ventricular afterload leading to left ventricular hypertrophy (LVH) and diastolic dysfunction. However, emerging models attribute the development of HFpEF to systemic proinflammatory changes secondary to common comorbidities which include HTN. Alterations in passive ventricular stiffness, ventricular-arterial coupling, peripheral microvascular function, systolic reserve, and chronotropic response occur.[32]

The central paradigm involves a systemic proinflammatory state triggering a downstream cascade of cardiac microvascular endothelial activation, oxidative stress, and abnormal myocardial cyclic guanosine monophosphate signaling, leading to microvascular rarefaction, chronic ischemia, fibrosis and progression to HFpEF.[33]

In a study conducted by Obokata M et al[34], N-Terminal pro-B type natriuretic peptide levels were below the level considered to exclude disease (<=125 pg/mL) in 18% of subjects with HFpEF. E/e' ratio was correlated with directly measured pulmonary capillary wedge pressure at rest (r=0.63, P<0.0001) and during exercise (r=0.57, P<0.0001). Although specific, current guidelines were poorly sensitive, identifying only 34% to 60% of subjects with invasively proven HFpEF on the basis of resting echocardiographic data alone. Addition of exercise echocardiographic data (E/e' ratio>14) improved sensitivity (to 90%) and thus negative predictive value, but decreased specificity (71%).

Intense research has implicated multiple factors in the etiology of HFpEF syndrome including systemic inflammation, LV hypertrophy, slowed LV relaxation, increased LV stiffness and remodeling, increased peripheral vascular resistance, impaired endothelial dysfunction, increased pulmonary vascular resistance, and neurohormonal activation. Ventricular-arterial coupling has been suggested as a more unifying theory. When arterial circulation becomes “stiffer,” the afterload increase is responsible for elevated blood pressure and progressive loss of LV elasticity with higher filling pressures. Groups more prone to develop HFpEF include those with obesity, diabetes, hypertension, and chronic kidney disease.[35]

According to Donal E et al[36], stroke volume and its change during exercise should be also assessed. In fact, unlike in a normal compliant heart, there is no increase in left ventricular end-diastolic volume during exercise and consequently no increase in cardiac output in heart failure with preserved ejection fraction. The absence of increased cardiac output during exercise is, like E/e’ and estimated pulmonary artery pressure, a

major parameter to be investigated during submaximal exercise performed to confirm the diagnosis of heart failure with preserved ejection fraction as an etiology of dyspnea.

All imaging techniques can provide an ejection fraction, but the versatility of echocardiography makes it unique in the provision of volumes, diastolic function, right ventricular function, hemodynamics, and valvular regurgitation. The early detection of heart failure has been facilitated by the assessment of global longitudinal strain, which is also useful in later heart failure for the assessment of left ventricular synchrony. The use of echocardiography has been associated with favorable outcomes, probably on the basis of facilitation of appropriate therapy.[37]

Echocardiography remains an essential procedure in HF. Echocardiography allows for accurate diagnosis and prognosis in both HFrEF and also in HFpEF. Future research should focus on combining echocardiographic prognostic markers into easily applicable prediction models in order to aid clinical decision making.[38]

Recent publications suggest that diastolic dysfunction is the primary cause of heart failure in 30-50% of patients[39]. Several studies also show that, in a significant number of patients with systolic dysfunction, diastolic function is the major determinant of their symptomatic status, their response to treatment and their outcome. Other preliminary data suggest that diastolic dysfunction is an important cause of exercise intolerance in patients with chronic hypertension.[39]

Plasma BNP levels were lower and associated with predominantly LV concentric remodeling/hypertrophy, presumably derived from age-related higher systolic and pulse pressures or aortic stiffness in the HFpEF patients than in the HFrEF patients, who were associated predominantly with eccentric hypertrophy. The results imply that LV concentric remodeling/hypertrophy and hence less end diastolic wall stress stimulates less BNP production in HFpEF as compared with HFrEF. These findings strongly suggest that the pathogenesis and hence

management of HFpEF may be distinct from those of HFrEF.[40] Patients with HFpEF have impaired LV long-axis systolic function, which can be measured using mitral annular systolic excursion or systolic velocities or LV global longitudinal strain (GLS).[41]

A study from the CHARM echocardiographic substudy-CHARMES done by Hans Persson et al [42] demonstrated that moderate and severe diastolic dysfunction (DD) were important predictors of adverse outcome. Patients underwent Doppler echocardiographic examination that included assessment of pulmonary venous flow or determination of plasma NT-pro-brain natriuretic peptide >=14 months after randomization to candesartan or placebo. The patients were classified into 1 of 4 diastolic function groups: normal, relaxation abnormality (mild dysfunction), pseudonormal (moderate dysfunction), and restrictive (severe dysfunction). Moderate DD (hazard ratio 3.7, 95% confidence interval [CI] 1.2 to 11.1) and severe DD (HR 5.7, 95% CI 1.4 to 24.0) remained the only independent predictors ($p<0.003$). The results demonstrated the prognostic significance and need for objective evidence of DD in HF patients. The study also showed that moderate and severe DD had a poor outcome compared to normal and mild DD (18% vs. 5%, $p<0.01$).

Cut-offs for key non-invasive parameters are often based on limited data, and may fall in a non-diagnostic intermediate range.[43] The non invasive diagnosis or exclusion of HFpEF will not depend on a single parameter above or below a certain cut-off, but on a combination of parameters derived from clinical, laboratory, and imaging tests that together will give a probability for the diagnosis. A recent example of such an approach was a composite HFpEF diagnostic score, derived retrospectively from clinical characteristics (age > 60 years, obesity, atrial fibrillation, treatment with >_2 antihypertensive drugs) and echocardiographic measurements [E/e'>9, pulmonary artery systolic pressure (PASP) >35 mmHg].[43]

MATERIALS AND METHODS

A hospital based observational study was conducted of 150 cases from OPD of DMCH from March 2020 to May 2021. The cases were divided into 2 groups:

Group A- The first group, group A, contained 75 cases with suspected HFpEF which is defined as patients presenting with symptoms of dyspnea, chest pain or palpitations only on exertion and not at rest, have left ventricular ejection fraction >=50% at rest, septal E/e' at rest 9–14, and BNP at rest 50-200 pg/ml. Group A cases were normotensive.

Group B- The second group, group B, contained 75 asymptomatic cases with arterial hypertension and left ventricular ejection fraction >=50% at rest with septal E/e' ratio <=14 at rest and BNP 50-200pg/ml.

The study population was investigated with CBC, ECG, creatinine, BNP, albumin, lipid profile, RBS and then subsequently an echocardiography was done at rest. Those with a normal echocardiography then got treadmill test (TMT). After the completion of prespecified end points of TMT according to Bruce protocol[44], patients were immediately shifted to echo table for DST echocardiography. Wall motion analysis and E/e' ratio was measured. The patients which had an E/e' ratio of >14 on DST echocardiography were considered to have abnormal DST echocardiography and were diagnosed with HFpEF+ on stress. The patients in which E/e' ratio remained <=14 on DST echocardiography were considered to have a normal DST echocardiography and were designated as HFpEF- on stress.

The results obtained were studied as to the proportion of cases in each group to develop HFpEF during DST echocardiography. Patients that developed ischemic changes on TMT or RWMA on DST echocardiography were excluded from the study. The findings of blood reports and urine routine analysis were analyzed and compared between those who developed HFpEF on stress and those who did not.

The study included a written proforma which had epidemiological information such as age, sex, occupation and place of residence, present history of complaints and past history of similar complaints and comorbidities, general and systemic examination, diagnosis and routine investigations, BNP levels and resting and diastolic stress echocargiographic findings.

INCLUSION CRITERIA:

- Age 18 years and above
- Normal ECG and echocardiography at rest
- Willing to give consent for the study

EXCLUSION CRITERIA:

- Age less than 18 years
- Patients with history of MI or any other heart disease
- Cardiac arrhythmias or pericardial diseases
- Abnormal 2-D echocardiography study or with EF<50%
- CKD or CLD
- ECG presence of pathological Q wave, LBBB, RBBB, AV block, ST-T changes.
- Structural heart diseases like cardiomyopathies and valvular heart defects
- Prior coronary intervention
- BNP <50 pg/ml or BNP>200pg/ml
- Symptoms of heart failure at rest
- Evidence of ischemic changes on TMT or RWMA on DST echo
- Anemia with Hb less than 8 g/dl
- Respiratory diseases like COPD
- Not willing to give consent for the study
- Coronary Artery Disease

DURATION OF STUDY – 15 months.

SAMPLE SIZE – 150 cases.

METHODOLDGY – 150 cases were studied. 75 cases in each of the 2 groups already mentioned above. The following parameters were considered:

- Hb:
- TLC:
- RBS:
- RFT:
- LFT:
- LIPID PROFILE:
- BNP:
- URINE ROUTINE:
- 2-D ECHO:
- DIASTOLIC STRESS ECHO:

The findings were studied and the proportion of cases which developed HFpEF during DST echocardiography in each group was analyzed.

PROCEDURE –

- Blood tests, ECG and urine analysis was done.
- Conventional echocardiography was done.
- Treadmill test was performed with GE CASE machine using Bruce protocol.[44]
- Stress echocardiography was performed using a standard ultrasound system (PHILIPS iE33) with a 1-5 MHz transducer at 1st min of recovery.
- Patients were studied in left lateral position using Philips iE33 using 1-5 MHz and baseline parameters were obtained before TMT. After the completion of prespecified end points of TMT, patient was immediately shifted to echo table which was available by the side of TMT. Wall motion analysis and E/e' ratio was measured.

OBSERVATION AND RESULTS

Table 1- Percentage of cases to develop HFpEF on stress in group A

HFpEF in DST Echo	No. of cases	%age
N	33	44.0%
Y	42	56.0%
Total	75	100.0%

Out of 75 cases in group A, 42 tested HFpEF+ on stress with E/e'>14 which accounts to 56%. 33 cases or 44% tested HFpEF- on stress.

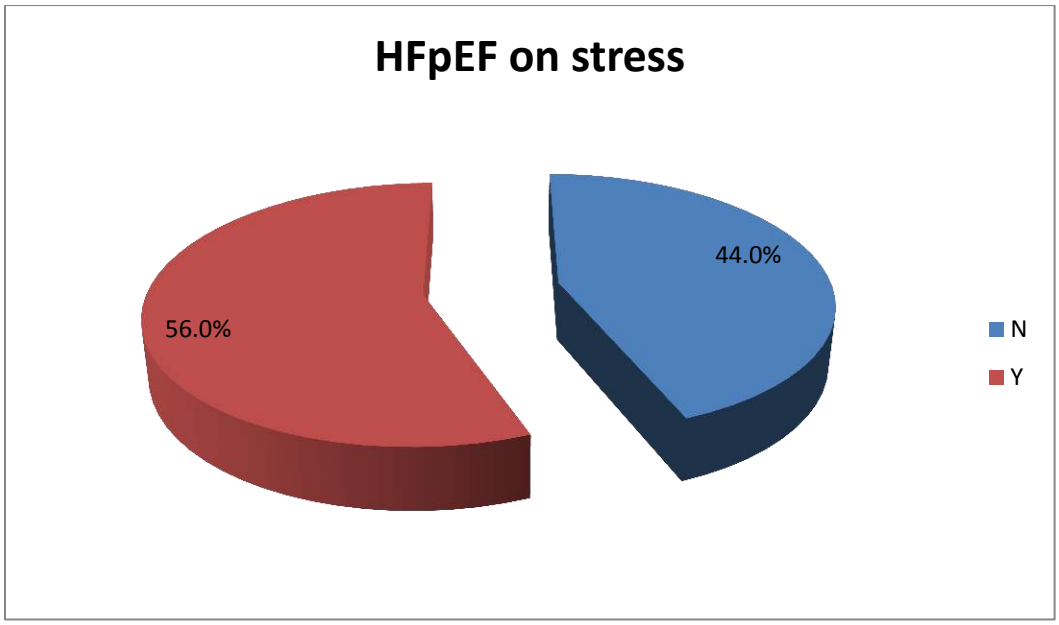

Figure 1- Percentage of cases to develop HFpEF on stress in group A

Table 2- Age distribution in group A

Age	HFpEF- on stress		HFpEF+ on stress		Total
< 30	6	18.2%	4	9.5%	10
31-40	7	21.2%	12	28.6%	19
41-50	10	30.3%	15	35.7%	25
51-60	7	21.2%	8	19.0%	15
61-70	3	9.1%	3	7.1%	6
Total	33	100.0%	42	100.0%	75

In group A, the mean age was 54.11±11.6 years. The cases that tested HFpEF+ on stress had mean age of 54.02 with SD 10.01 and the cases that tested HFpEF- on stress had mean age of 54.21 with SD 12.44 years.

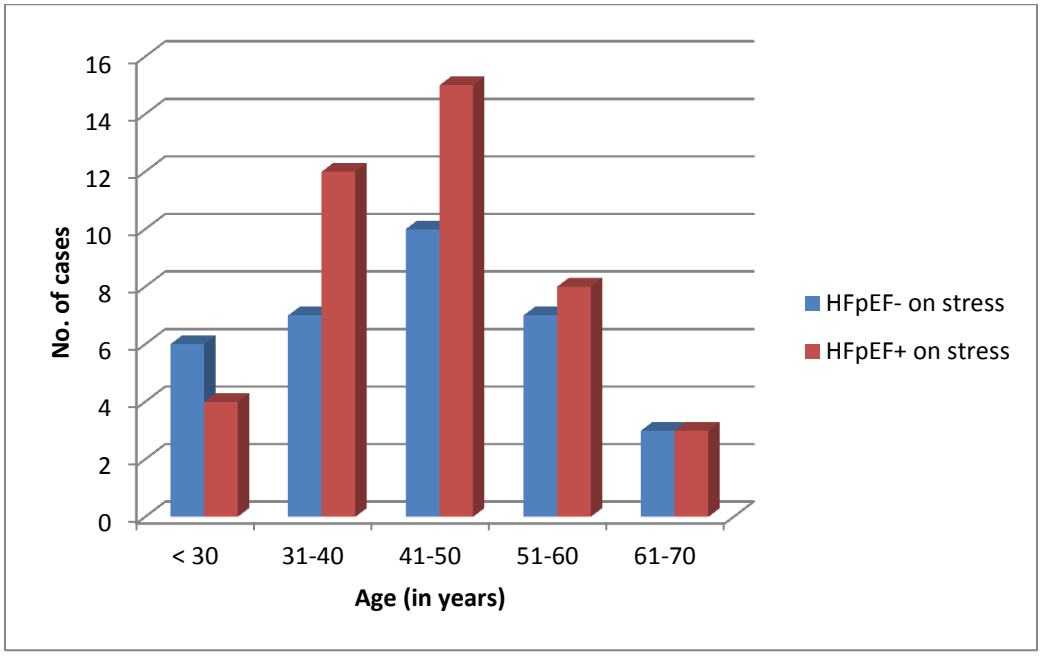

Figure 2- Age distribution in group A

Table 3- Gender distribution in group A

Sex	HFpEF- on stress		HFpEF+ on stress		Total
F	12	36.4%	14	33.3%	26
M	21	63.6%	28	66.7%	49
Total	33	100.0%	42	100.0%	75

In group A, 65.3% cases were males.

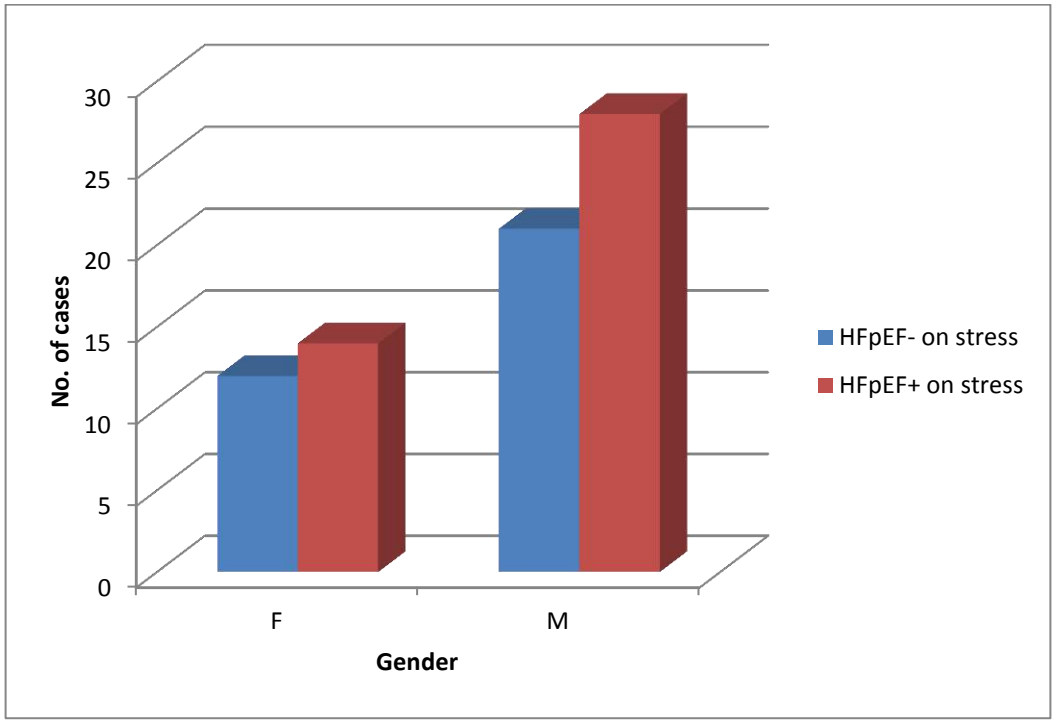

Figure 3- Gender distribution in group A

Table 4- Diabetes distribution in group A

Diabetes Mellitus	HFpEF- on stress		HFpEF+ on stress		Total	p-value
N	27	81.8%	11	26.2%	38	0.001
Y	6	18.2%	31	73.8%	37	
Total	33	100.0%	42	100.0%	75	

For the 42 cases that tested HFpEF+ on stress, 73.8% (31 cases) were diabetic. For the 33 cases that tested HFpEF- on stress, 81.1% (27 cases) were non-diabetic. This data shows correlation of diabetes mellitus with abnormal DST echocardiography with statistically significant p-value of 0.001.

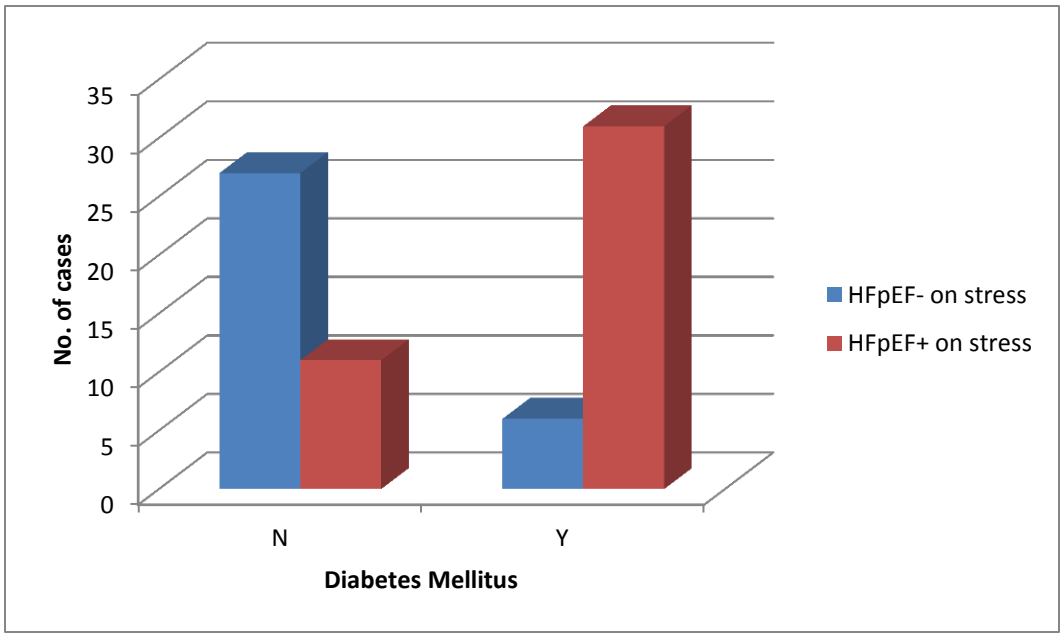

Figure 4- Diabetes distribution in group A

Table 5- Alcohol intake distribution in group A

Alcohol intake	HFpEF- on stress		HFpEF+ on stress		Total	p-value
N	25	75.8%	31	73.8%	56	0.847
Y	8	24.2%	11	26.2%	19	
Total	33	100.0%	42	100.0%	75	

Of the cases that tested HFpEF+ on stress, 26.2% had a history of alcohol consumption. Of the cases which tested HFpEF- on stress, 24.2% consumed alcohol. Alcohol intake was statistically not significant with a p-value of 0.847.

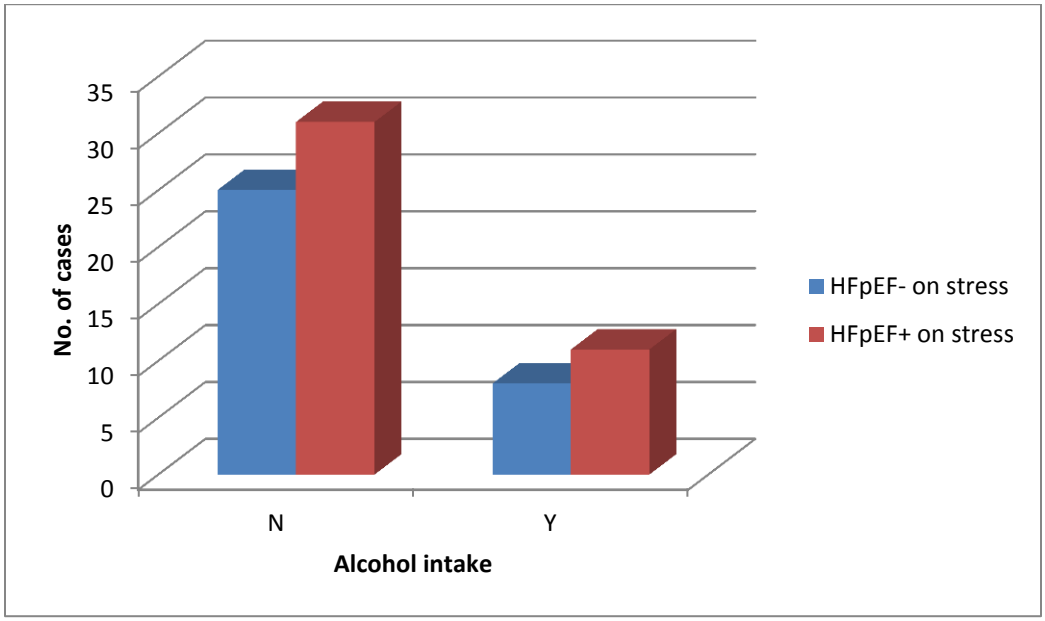

Figure 5- Alcohol intake distribution in group A

Table 6- Smoking distribution in group A

Smoking	HFpEF- on stress		HFpEF+ on stress		Total	p-value
N	31	93.9%	26	61.9%	57	0.0001
Y	2	6.1%	16	38.1%	18	
Total	33	100.0%	42	100.0%	75	

In group A, out of 18 cases with a history of smoking, 16 tested HFpEF+ on stress which means that 89.9% of smokers tested HFpEF+. 16 (38.1%) out of 42 cases which tested HFpEF+ on stress were smokers whereas only 2 (6.1%) out of 33 cases which tested HFpEF- on stress were smokers. This data is statistically significant with a p-value of 0.0001.

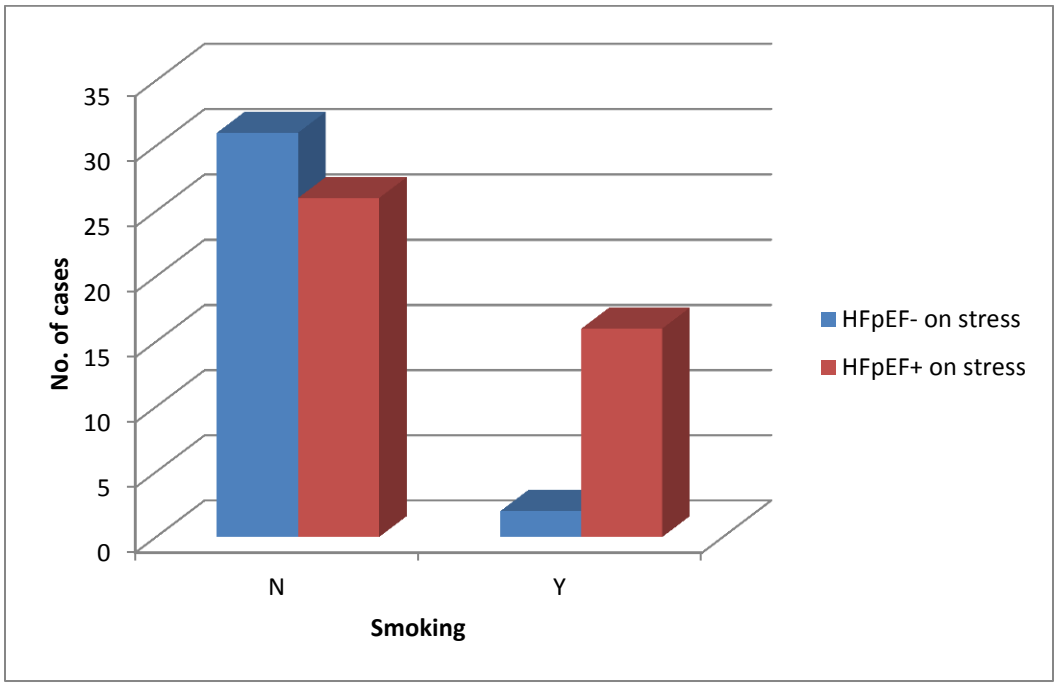

Figure 6- Smoking distribution in group A

Table 7- Proteinuria distribution in group A

		HFpEF- on stress		HFpEF+ on stress		Total	p-value
Proteinuria (Y/N)	N	30	90.9%	17	40.5%	47	0.0001
	Y	3	9.1%	25	59.5%	28	
Total		33	100.0%	42	100.0%	75	

Out of 42 cases that tested HFpEF+ on stress, 25 cases or 59.5% had proteinuria, whereas out of 33 cases that tested HFpEF- on stress, only 3 cases or 9.1% had proteinuria. Presence of proteinuria was a statistically significant factor for abnormal DST echocardiography with a p-value of 0.0001.

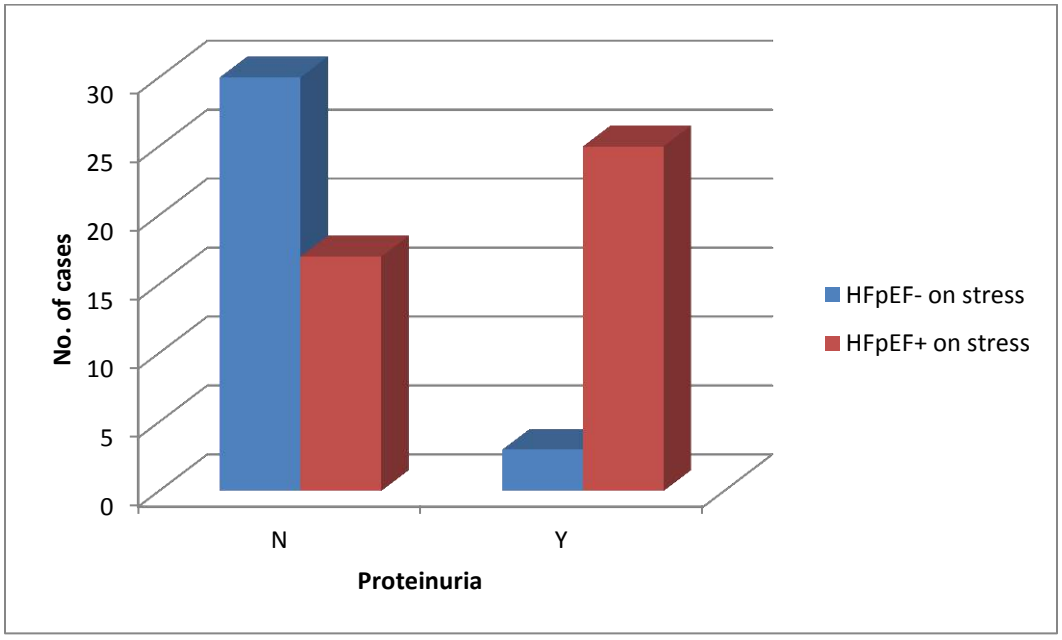

Figure 7- Proteinuria distribution in group A

Table 8- Glycosuria distribution in group A

		HFpEF- on stress		HFpEF+ on stress		Total	p-value
Glycosuria (Y/N)	N	27	81.8%	24	57.1%	51	0.023
	Y	6	18.2%	18	42.9%	24	
Total		33	100.0%	42	100.0%	75	

Out of 42 cases that tested HFpEF+ on stress, 18 (42.9%) had glycosuria whereas out of 33 cases that tested HFpEF- on stress, only 6 (18.2%) had glycosuria. This shows that glycosuria is statistically significant with a p-value of 0.023.

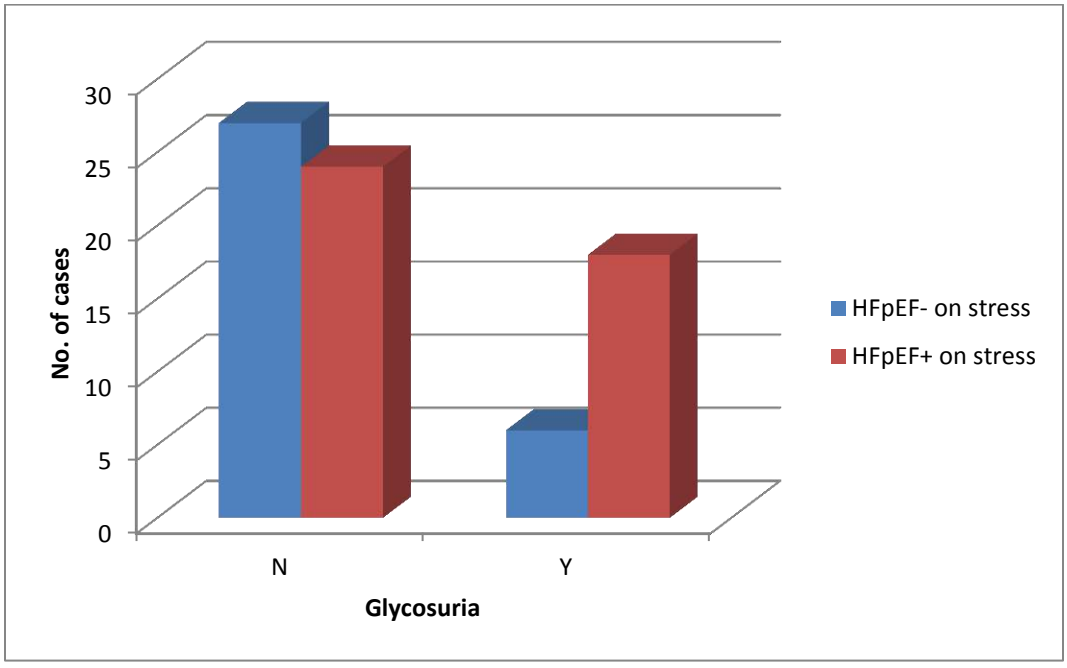

Figure 8- Glycosuria distribution in group A

Table 9- Distribution of vitals in group A

	HFpEF- on stress		HFpEF+ on stress			
	MEAN	SD	MEAN	SD		p-value
SBP (mm of Hg)	117.58	6.63	117.14	5.54	0.308	0.759
DBP (mm of Hg)	75.15	6.19	75.95	4.97	-0.622	0.536
HR (/min)	76.73	4.76	76.93	3.70	-0.206	0.837
Spo2% (in %)	98.18	1.55	98.05	1.56	0.371	0.712

In cases that tested HFpEF- on stress, means of SBP, DBP, HR and Spo2% were 117.58, 75.15, 76.73, and 98.18 with SD of 6.63, 6.19, 4.76 and 1.55 respectively. In cases that tested HFpEF+ on stress, means of SBP, DBP, HR and Spo2% were 117.14, 75.95, 76.93 and 98.05 respectively with SD of 5.54, 4.97, 3.70 and 1.56 respectively. This data was statistically not significant.

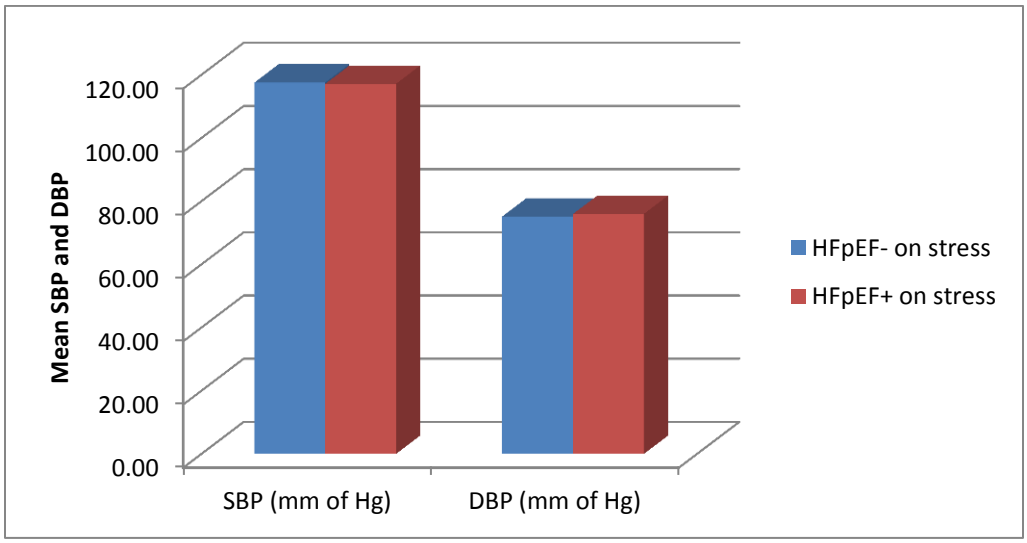

Figure 9- Distribution of systolic and diastolic BP in group A

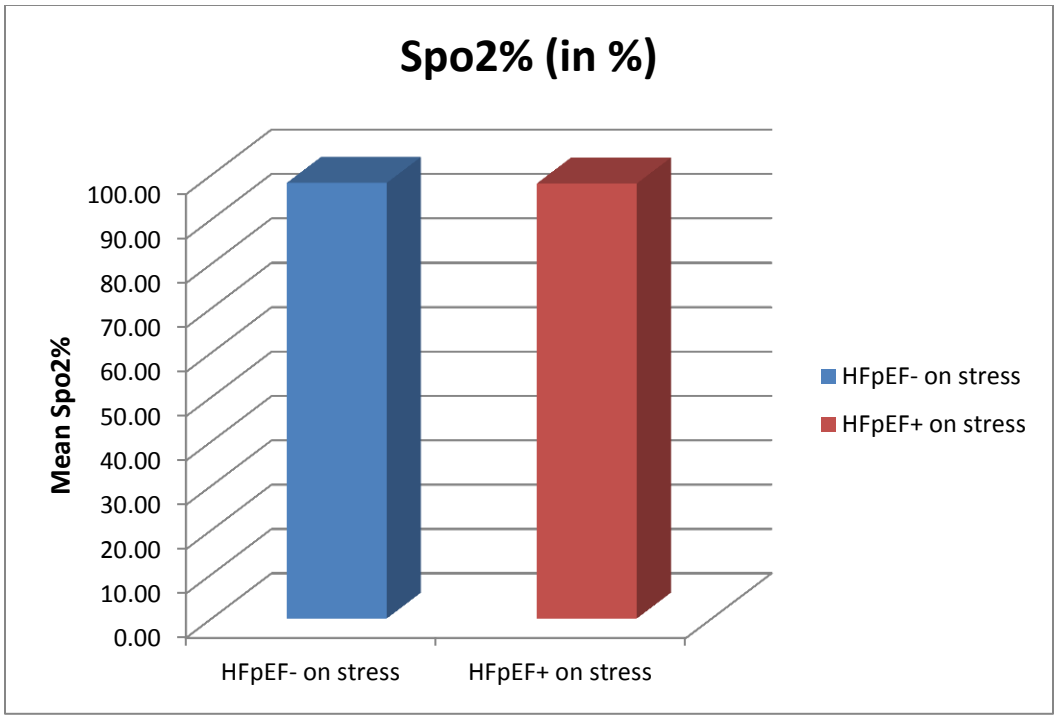

Figure 10- Distribution of spo2 in group A

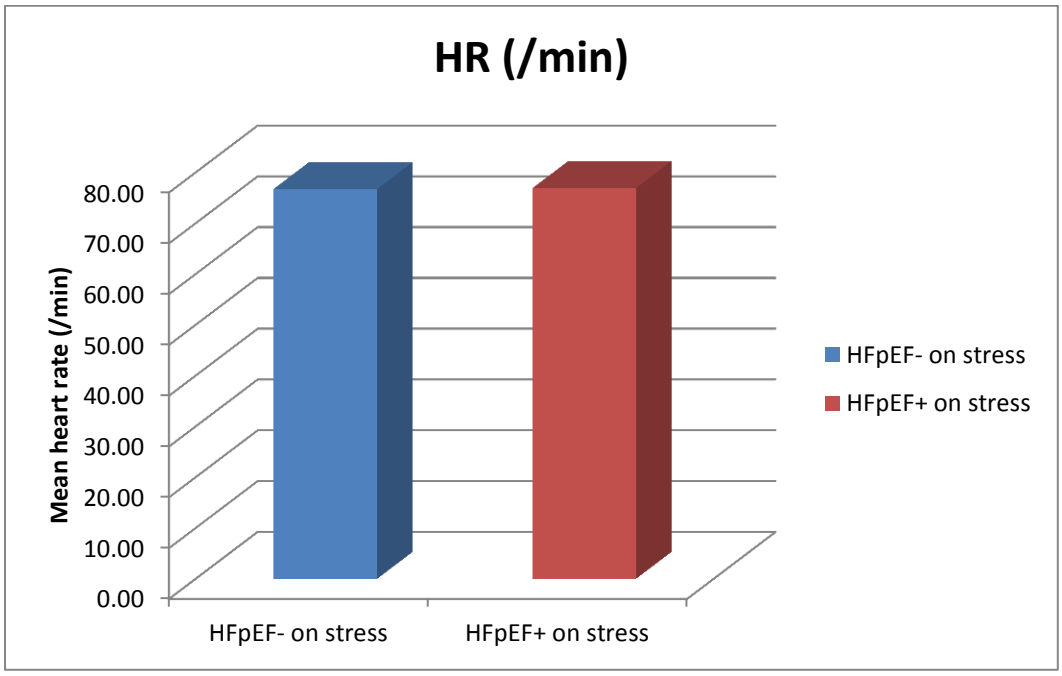

Figure 11- Distribution of HR in group A

Table 10- BMI distribution in group A

	HFpEF- on stress		HFpEF+ on stress		
	MEAN	SD	MEAN	SD	p-value
BMI (kg/m2)	22.44	3.22	24.42	3.19	0.010

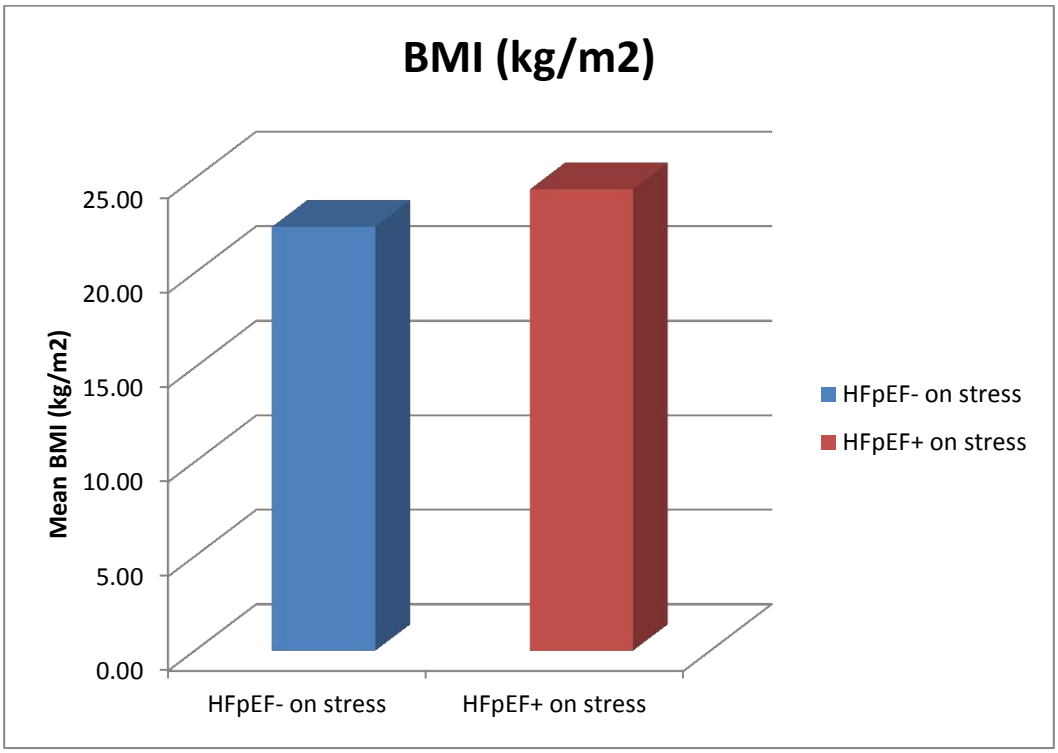

Figure 12- Mean BMI distribution in group A

Table 11- BMI distribution according to Asian criteria[45]

BMI (kg/m^2)	HFpEF- on stress		HFpEF+ on stress		Total
< 18.5	2	6.1%	0	0.0%	2
18.5-22.9	20	60.6%	13	31.0%	33
23-24.9	5	15.2%	13	31.0%	18
25-29.9	5	15.2%	14	33.3%	19
> 30	1	3.0%	2	4.8%	3
Total	33	100.0%	42	100.0%	75

In group A, cases which tested HFpEF+ on stress had a mean BMI of 24.42 with SD of 3.19 and cases which tested HFpEF- on stress had a mean BMI of 22.44 with SD of 3.22. BMI has a p-value of 0.010. Cases of BMI 23-24.9 and 25-29.9 kg/m^2 had highest proportion of cases that tested HFpEF+ on stress with 72.2% and 73.7% cases respectively belonging to these BMI ranges to test HFpEF+.

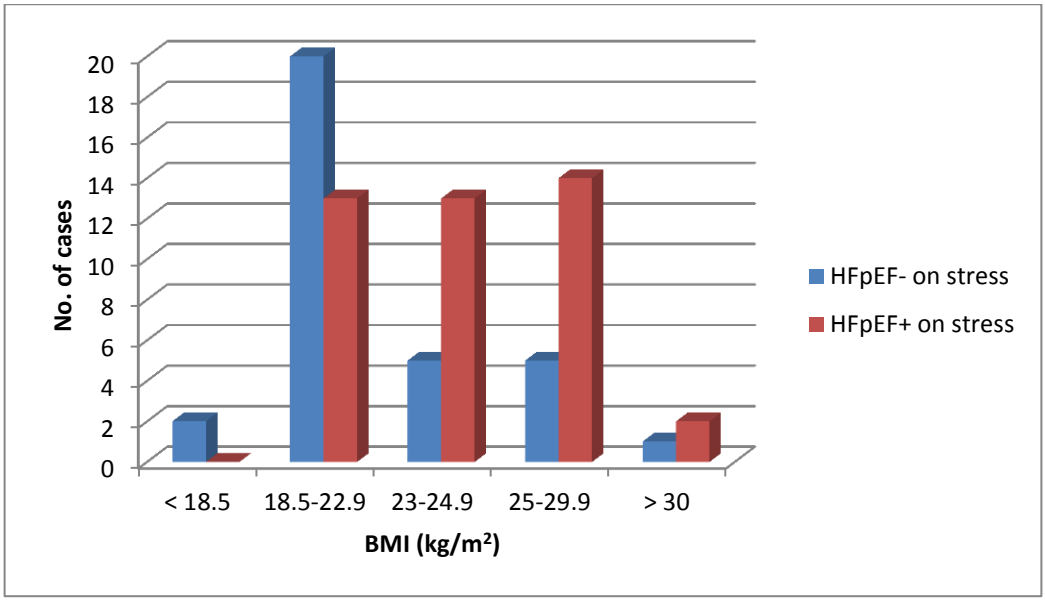

Figure 13- BMI distribution according to Asian criteria

Table 12- Lipid profile distribution in group A

	HFpEF- on stress		HFpEF+ on stress		
	MEAN	SD	MEAN	SD	p-value
Total Cholesterol (mg/dl)	168.00	43.03	233.90	41.41	0.000
TG (mg/dl)	151.82	27.48	209.38	43.98	0.000
HDL (mg/dl)	43.76	8.36	45.55	15.42	0.550
LDL (mg/dl)	113.58	27.07	157.02	47.12	0.000

The mean of total cholesterol, TG, HDL and LDL is higher in cases that tested HFpEF+ on stress. With respect to total cholesterol, it has a mean of 233.9 with SD 41.41 in cases which tested HFpEF+ on stress and it has a mean of 168.0 with SD 43.03 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to TG, it has a mean of 209.38 with SD 43.98 in cases which tested HFpEF+ on stress and it has a mean of 151.82 with SD 27.48 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to LDL, it has a mean of 157.02 with SD 47.12 in cases which tested HFpEF+ on stress and it has a mean of 113.58 with SD 27.07 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to HDL, it has a mean of 45.55 with SD 15.42 in cases which tested HFpEF+ on stress and it has a mean of 43.76 with SD 8.36 in cases which tested HFpEF- on stress. It has a p-value of 0.550.

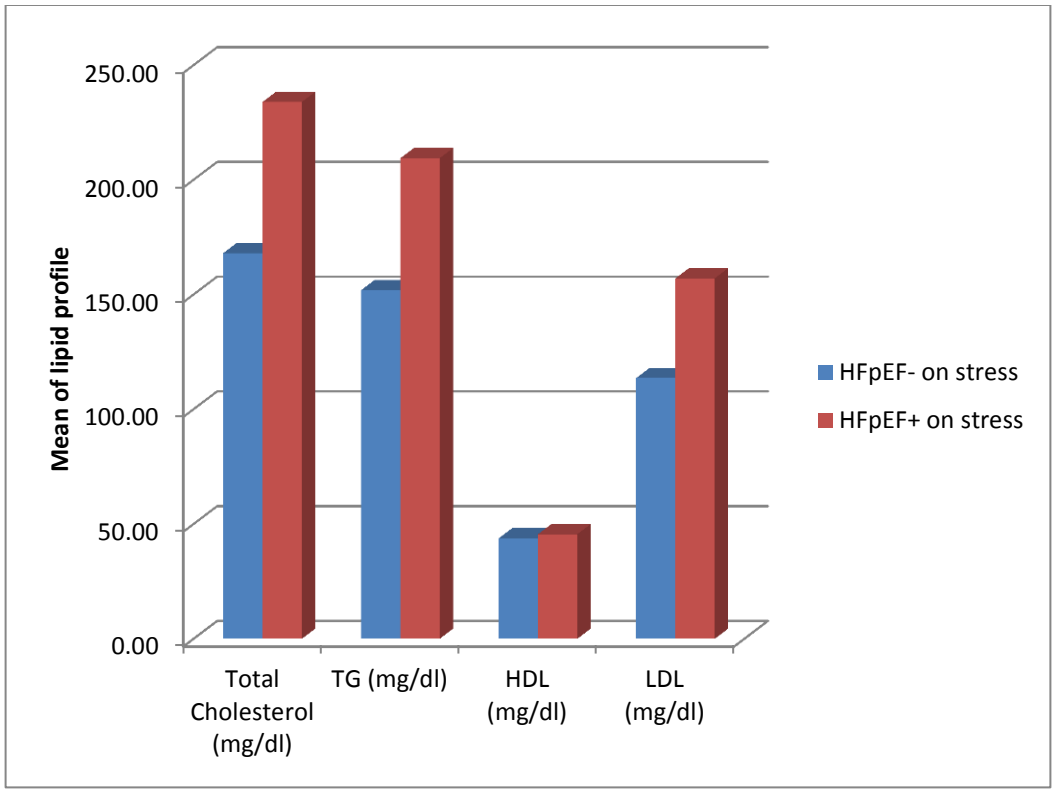

Figure 14- Lipid profile distribution in group A

Table 13- Hemogram, RFT, albumin distribution in group A

	HFpEF- on stress		HFpEF+ on stress		
	MEAN	SD	MEAN	SD	p-value
Hb (g/dl)	13.06	1.38	11.87	1.69	0.002
TLC (/mm3)	7.23	1.44	7.33	1.64	0.783
RBS (mg/dl)	105.06	49.99	172.45	69.32	0.000
Urea (mg/dl)	28.58	10.19	29.29	8.17	0.738
Creatinine (mg/dl)	0.66	0.25	0.66	0.27	0.987
Sodium (mmol/l)	137.24	4.70	143.50	3.10	0.000
Potassium (mmol/l)	3.92	0.35	3.91	0.39	0.953
Albumin (g/dl)	3.87	0.40	3.28	0.34	0.000

With respect to Hb, it has a mean of 11.87 with SD 1.69 in HFpEF+ cases and a mean of 13.06 with SD 1.38 in HFpEF- cases with a p-value of 0.002. With respect to TLC, it has a mean of 7.33 with SD 1.64 in HFpEF+ cases and a mean of 7.23 with SD 1.44 in HFpEF- cases with a p-value of 0.783. With respect to RBS, it has a mean of 172.45 with SD 69.32 in HFpEF+ cases and a mean of 105.06 with SD 49.99 in HFpEF- cases with a p-value of 0.000. With respect to urea, it has a mean of 29.29 with SD 8.17 in HFpEF+ cases and a mean of 28.58 with SD 10.19 in HFpEF- cases with a p-value of 0.738. With respect to creatinine, it has a mean of 0.66 with SD 0.27 in HFpEF+ cases and a mean of 0.66 with SD 0.25 in HFpEF- cases with a p-value of 0.987. With respect to sodium, it has a mean of 143.5 with SD 3.1 in HFpEF+ cases and a mean of 137.24 with SD 4.7 in HFpEF- cases with a p-value of 0.000. With respect to potassium, it has a mean of 3.91 with SD 0.39 in HFpEF+ cases and a mean of 3.92 with SD 0.35 in HFpEF- cases with a p-value of 0.953. With

respect to albumin, it has a mean of 3.28 with SD 0.34 in HFpEF+ cases and a mean of 3.87 with SD 0.4 in HFpEF- cases with a p-value of 0.000.

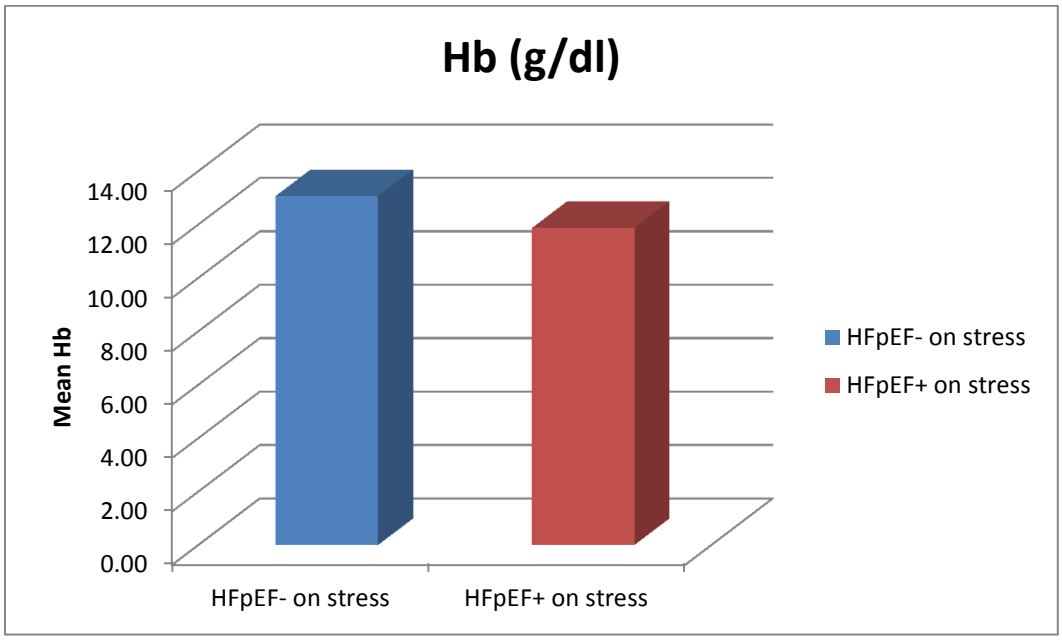

Figure 15- Mean Hb in group A

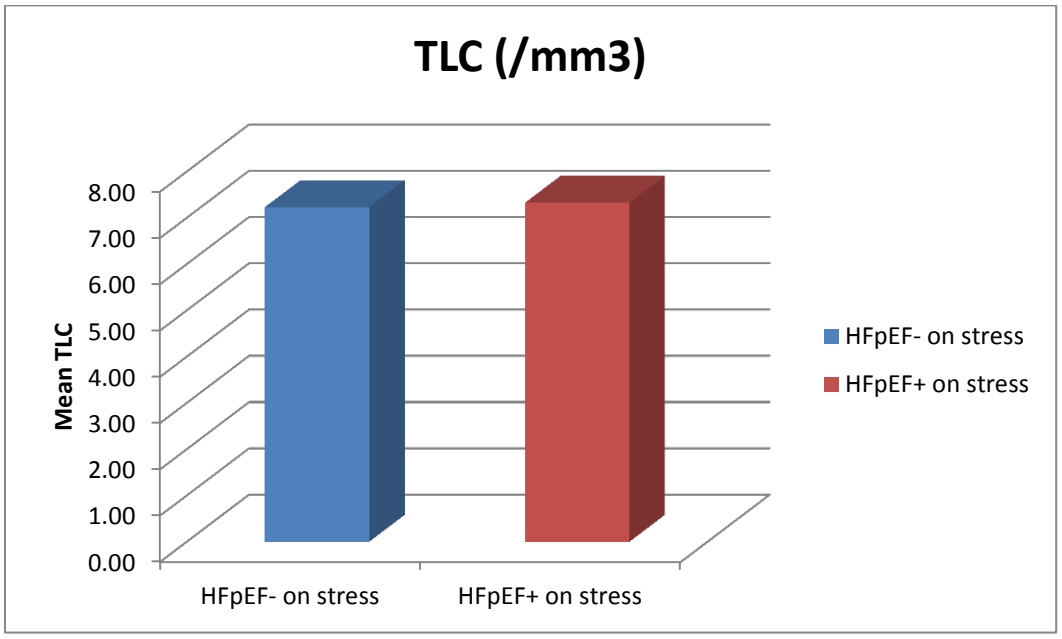

Figure 16- Mean TLC in group A

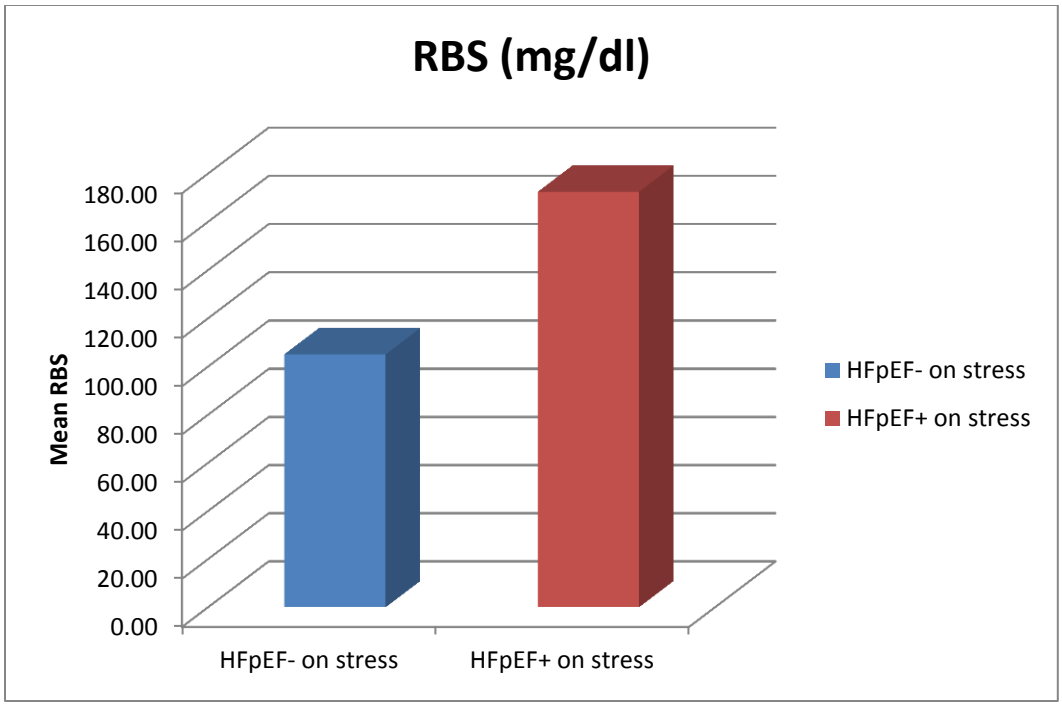

Figure 17- Mean RBS in group A

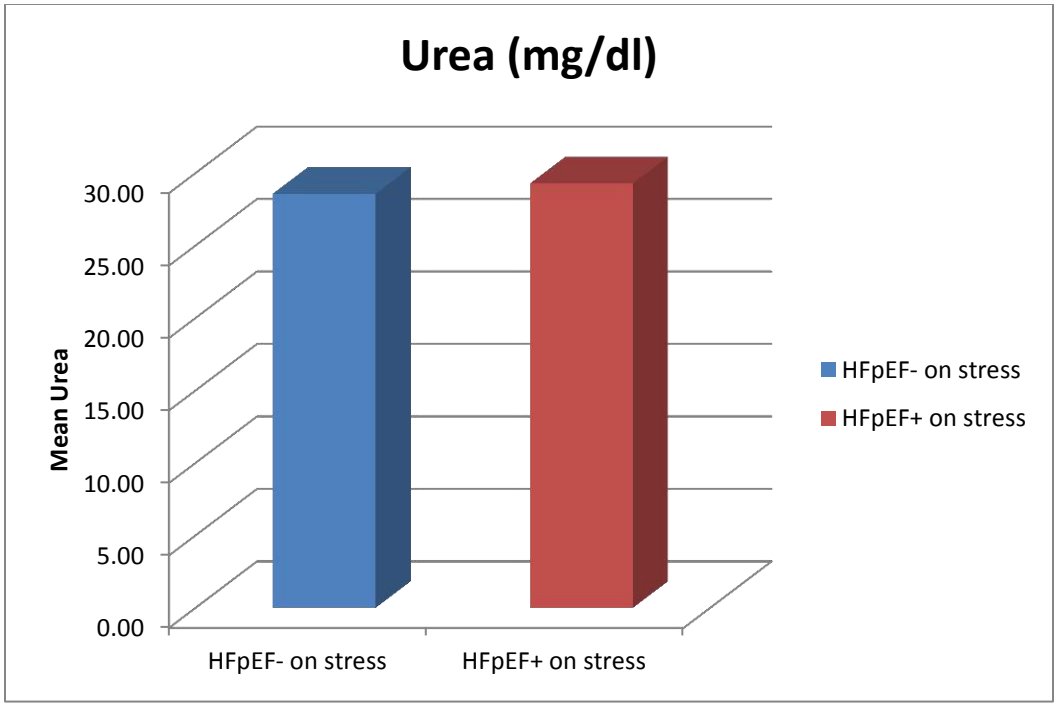

Figure 18- Mean urea in group A

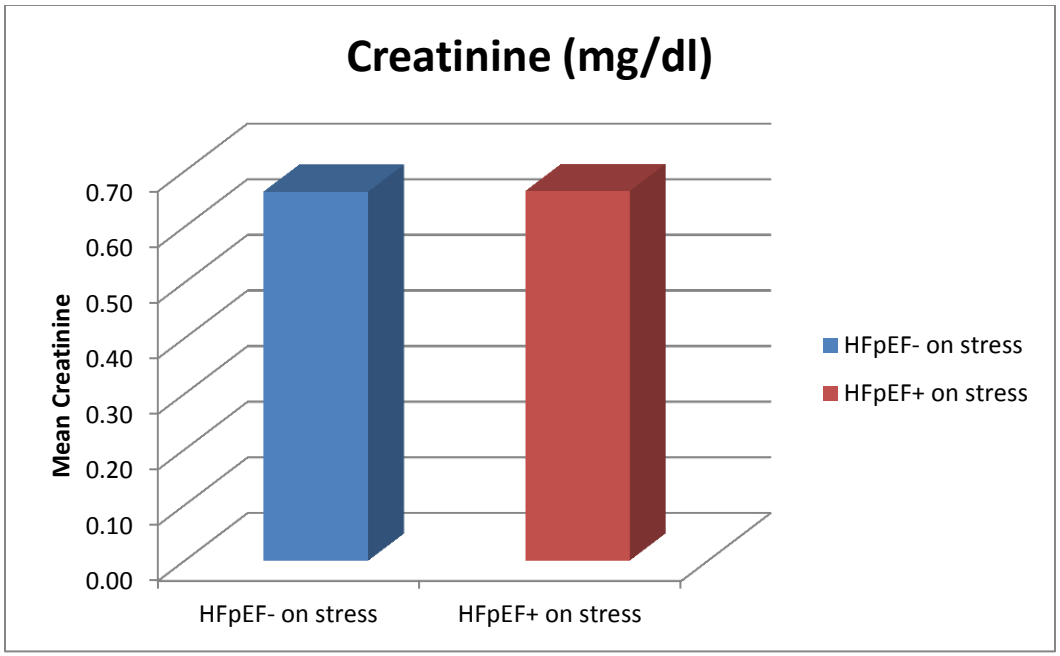

Figure 19- Mean creatinine in group A

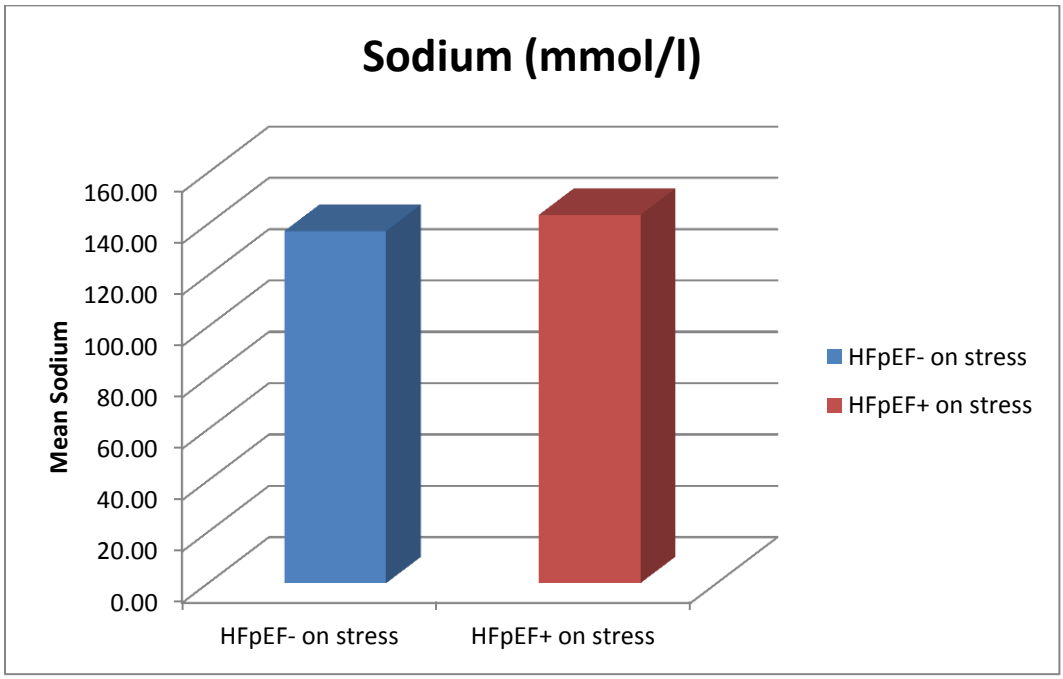

Figure 20- Mean sodium in group A

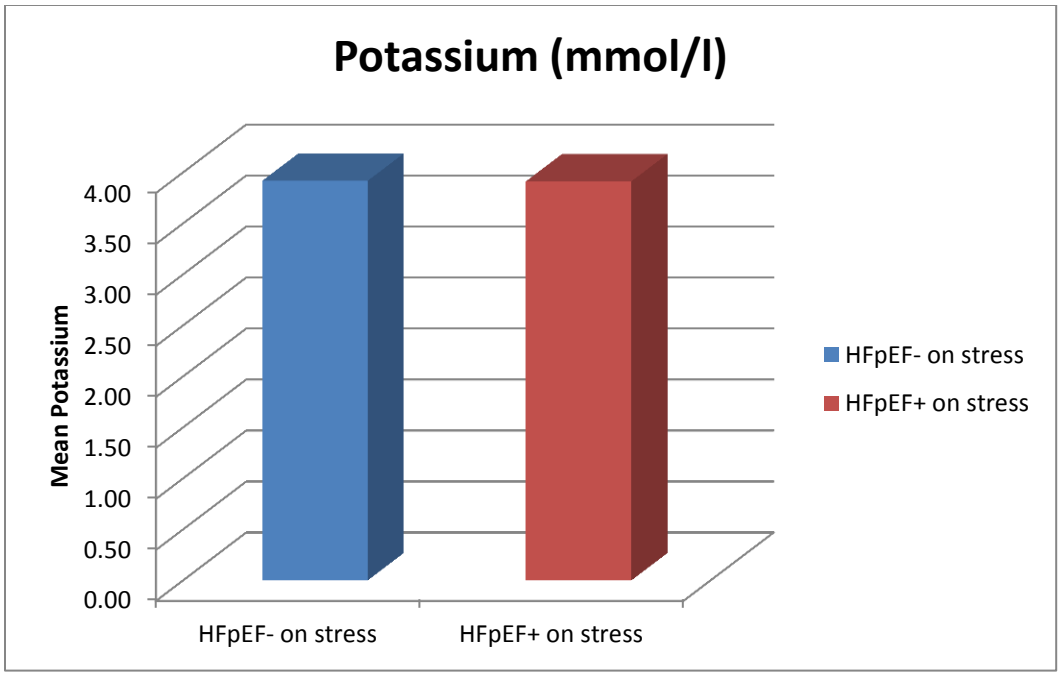

Figure 21- Mean potassium in group A

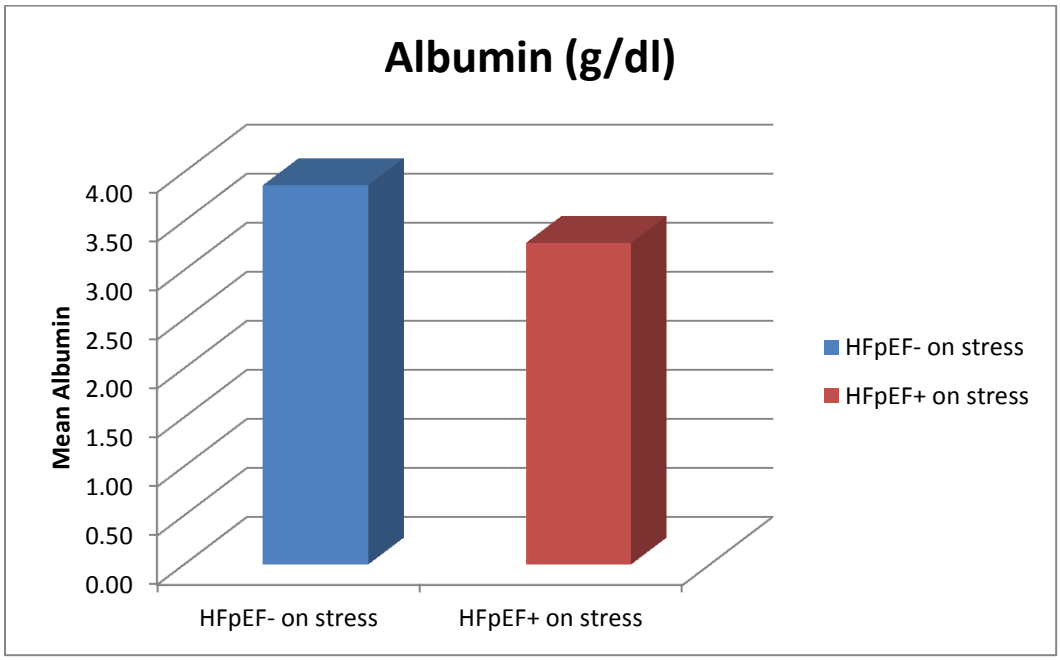

Figure 22- Mean albumin in group A

Table 14- BNP distribution in group A

	HFpEF- on stress		HFpEF+ on stress		
	MEAN	SD	MEAN	SD	p-value
BNP (pg/ml)	81.12	23.64	142.24	37.79	0.000

BNP has a mean of 142.24 with SD 37.79 in 42 cases which tested HFpEF+ on stress and a mean of 81.12 with SD 23.64 in 33 cases which tested HFpEF- on stress. P-value for BNP is 0.000.

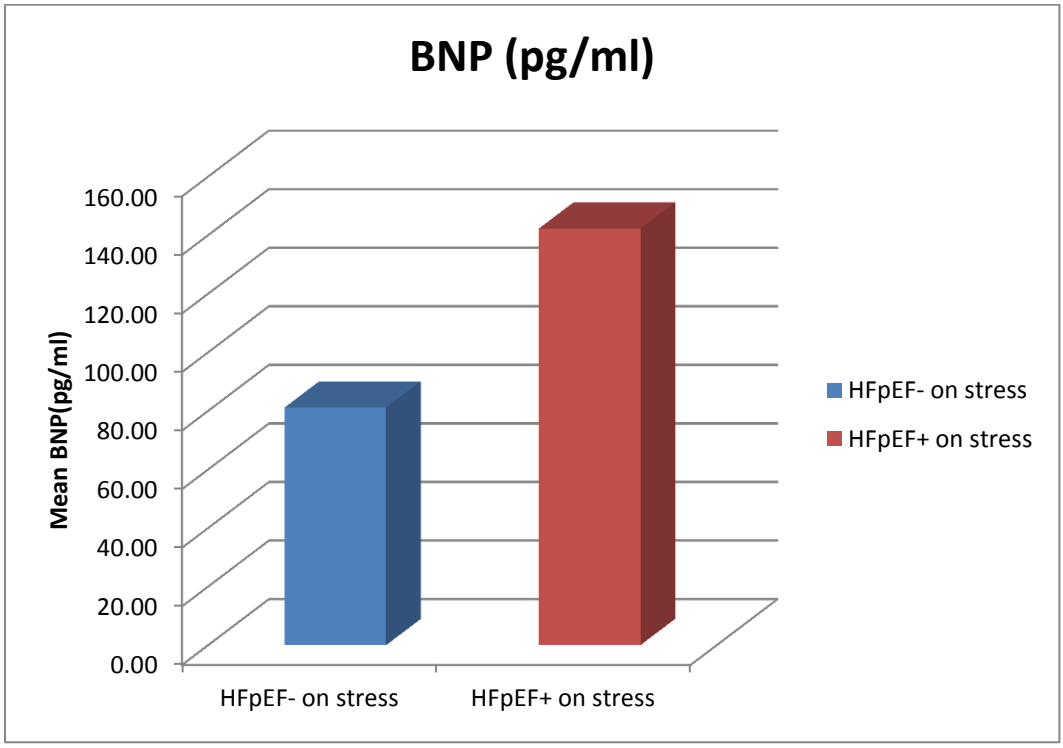

Figure 23- BNP distribution in group A

Table 15- Multivariate analysis of diabetes mellitus, smoking, BMI and Hb in group A

	p-value	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
Diabetes Mellitus	0.000	8.810	2.595	29.902
Smoking	0.168	3.679	0.578	23.436
BMI (kg/m2)	0.246	1.125	0.922	1.371
Hb (g/dl)	0.119	0.708	0.458	1.094

On multivariate logistic regression analysis involving diabetes mellitus, smoking, BMI and Hb. Diabetes mellitus was found to be the independent predictor of abnormal DST (OR=8.81, CI= 2.595- 29.902; p-value =0.000).

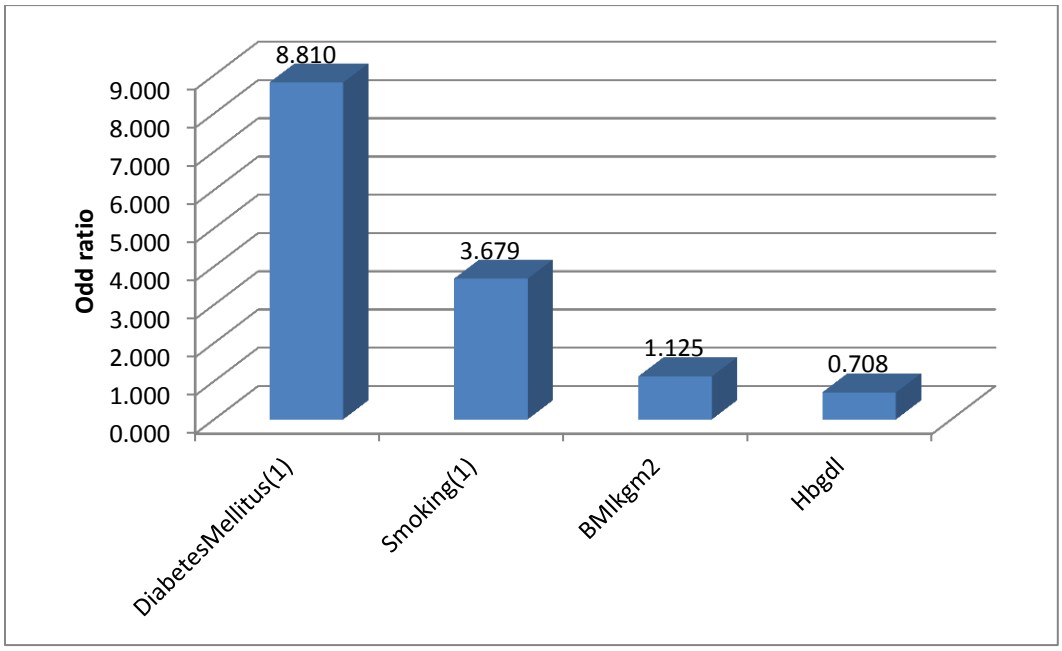

Figure 24- Multivariate analysis of diabetes mellitus, smoking, BMI and Hb in group A

Table 16- Percentage of cases to develop HFpEF on stress in group B

Diastolic failure in DST Echo (Y/N)	No. of cases	%age
N	73	97.3%
Y	2	2.7%
Total	75	100.0%

In group B, 2 out of 75 cases tested HFpEF+ on stress, which amounts to only 2.7% of the total cases.

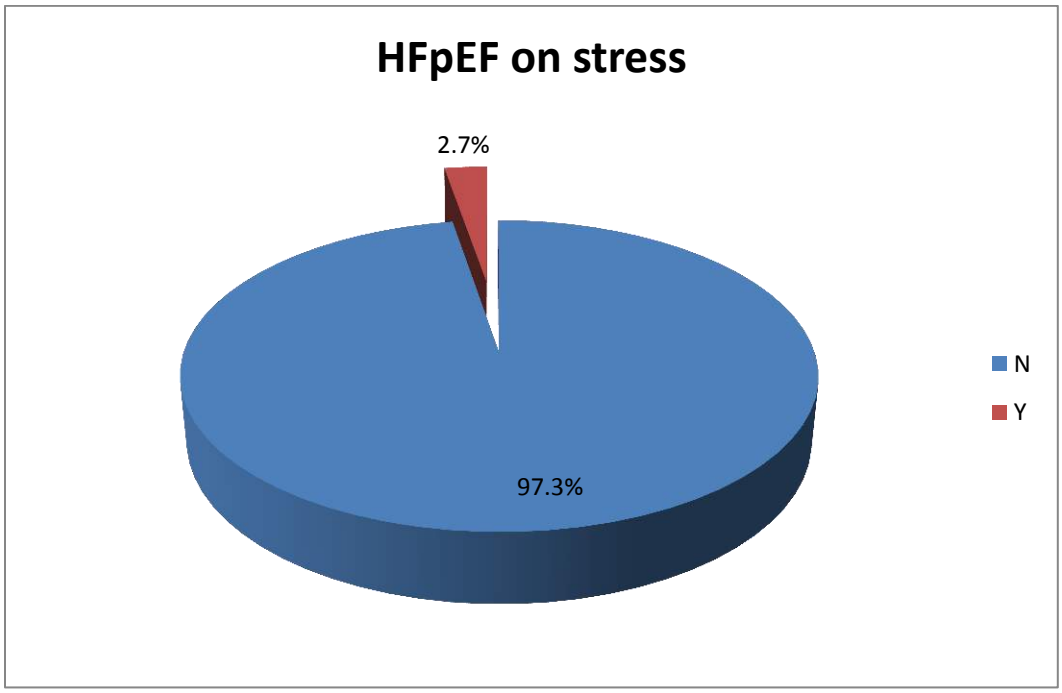

Figure 25- Percentage of cases to develop HFpEF on stress in group B

Table 17- Age distribution in group B

Age group	HFpEF- on stress		HFpEF+ on stress		**Total**
< 30	1	1%	0	0%	1
31-40	5	7%	1	50%	6
41-50	27	37%	0	0%	27
51-60	31	42%	1	50%	32
61-70	9	12%	0	0%	9
Total	73	100%	2	100%	75

The mean age in group B was 61.01±8.14 years.

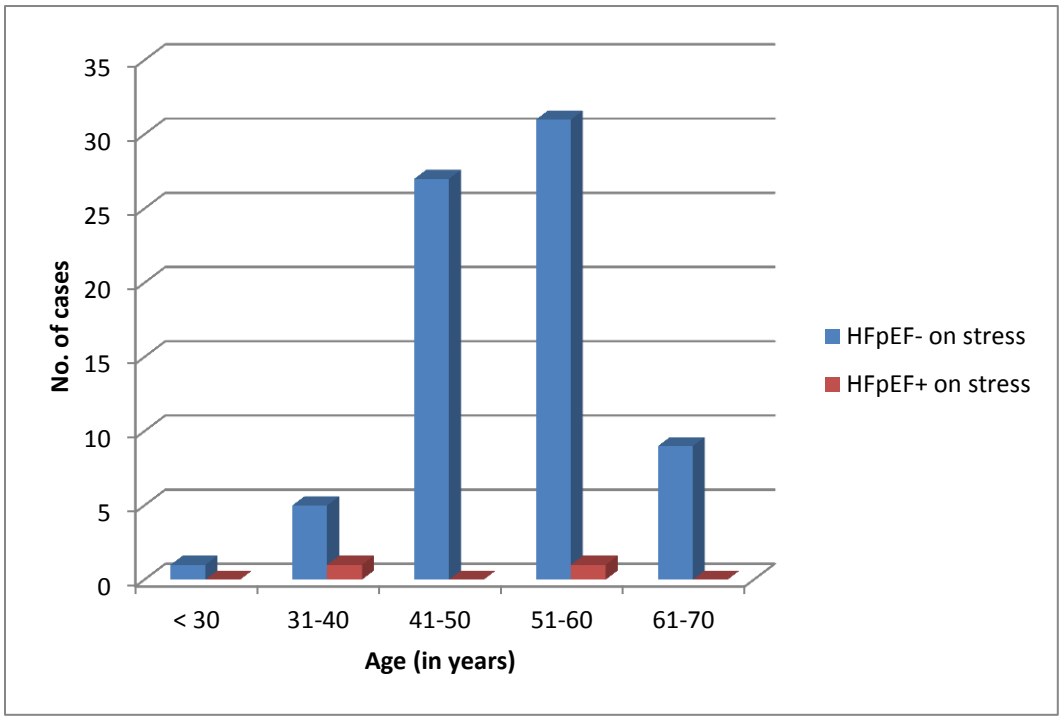

Figure 26- Age distribution in group B

Table 18- Gender distribution in group B

Sex	HFpEF- on stress		HFpEF+ on stress		Total
F	25	34%	1	50%	26
M	48	66%	1	50%	49
Total	73	100%	2	100%	75

65.3% of the cases in group B were males.

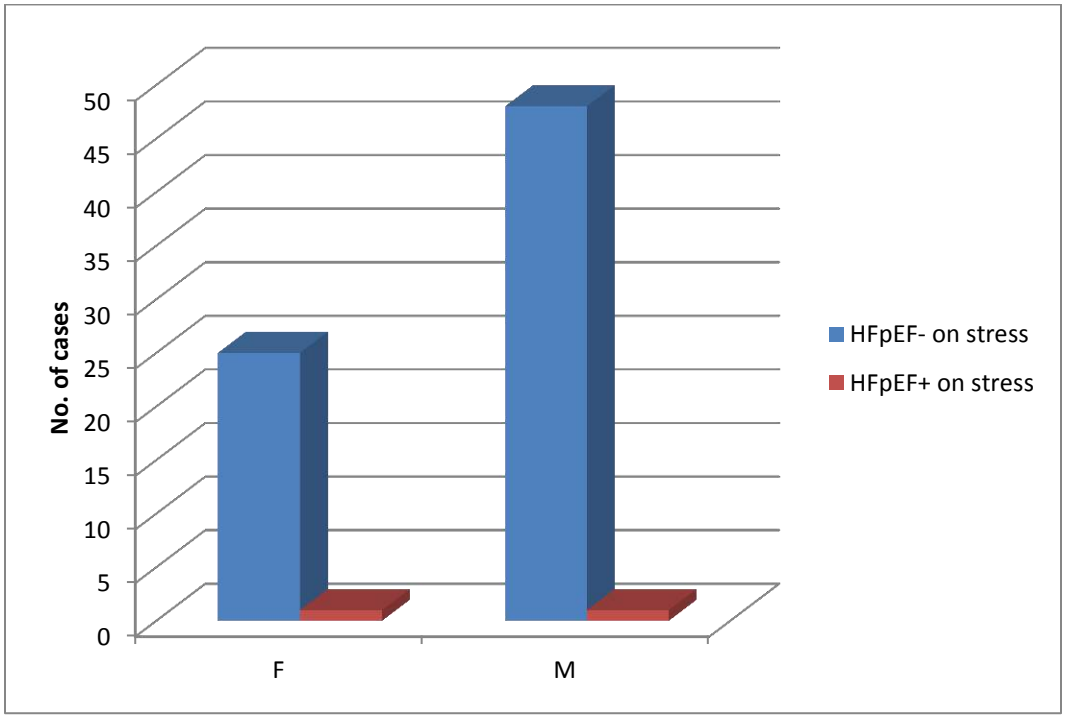

Figure 27- Gender distribution in group B

Table 19- Distribution of diabetes mellitus in group B

Diabetes Mellitus	HFpEF- on stress		HFpEF+ on stress		**Total**
N	38	52%	0	0%	38
Y	35	48%	2	100%	37
Total	73	100%	2	100%	75

Of the 2 cases in group B that tested HFpEF+ on stress, 100% were diabetic. Out of 73 cases that tested HFpEF- on stress, 48% had diabetes mellitus.

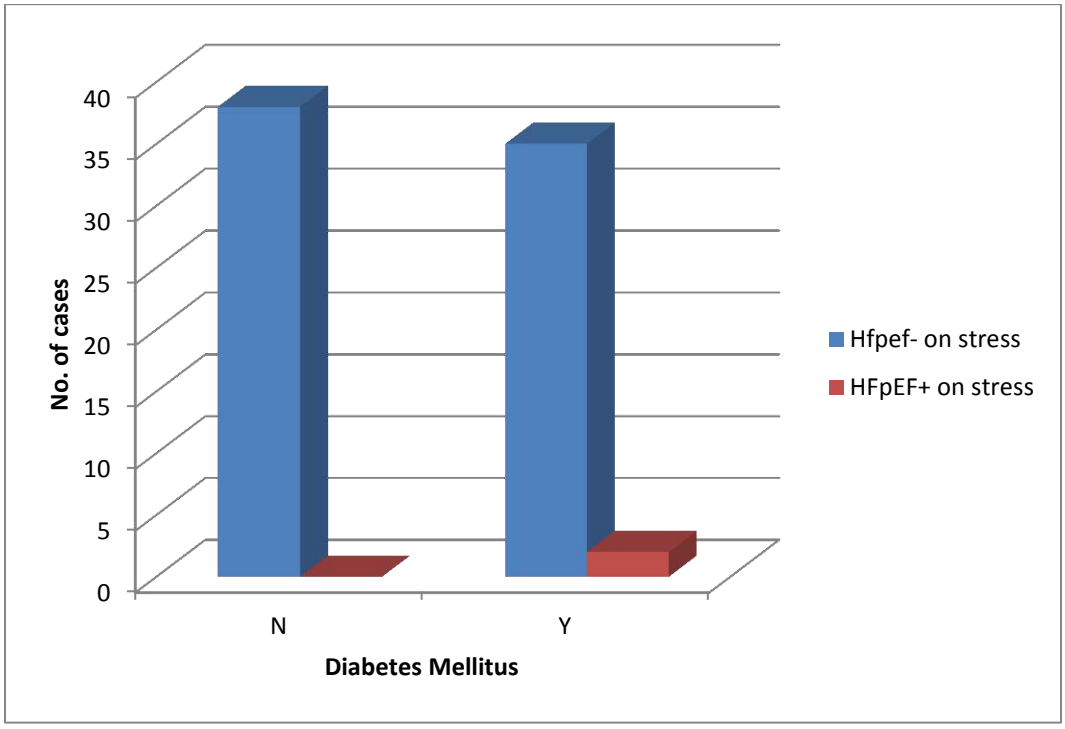

Figure 28- Distribution of diabetes mellitus in group B

Table 20- Distribution of alcohol intake in group B

Alcohol intake	HFpEF- on stress		HFpEF+ on stress		**Total**
N	56	77%	1	50%	57
Y	17	23%	1	50%	18
Total	73	100%	2	100%	75

Out of the 2 cases that tested HFpEF+ on stress, 1 had history of alcohol intake and 1 did not. Out of the 73 cases that tested HFpEF- on stress, 23% had history of alcohol intake.

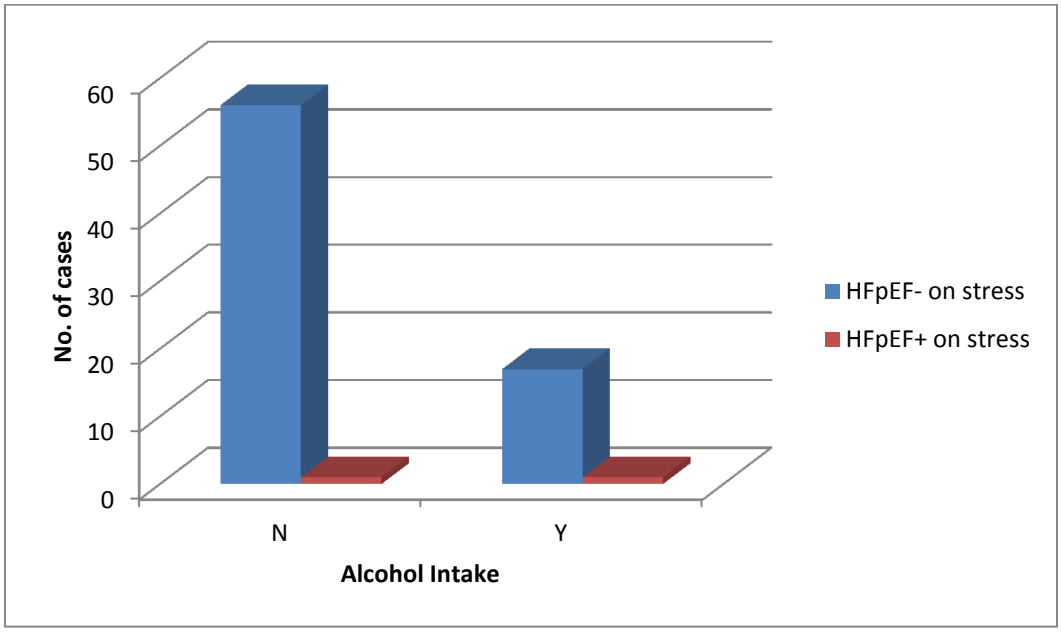

Figure 29- Distribution of alcohol intake in group B

Table 21- Distribution of smoking in group B

Smoking	HFpEF- on stress		HFpEF+ on stress		**Total**
N	53	73%	1	50%	54
Y	20	27%	1	50%	21
Total	73	100%	2	100%	75

Out of the 2 cases that tested HFpEF+ on stress, 1 had history of smoking and 1 did not. Out of the 73 cases that tested HFpEF- on stress, 27% had history of smoking.

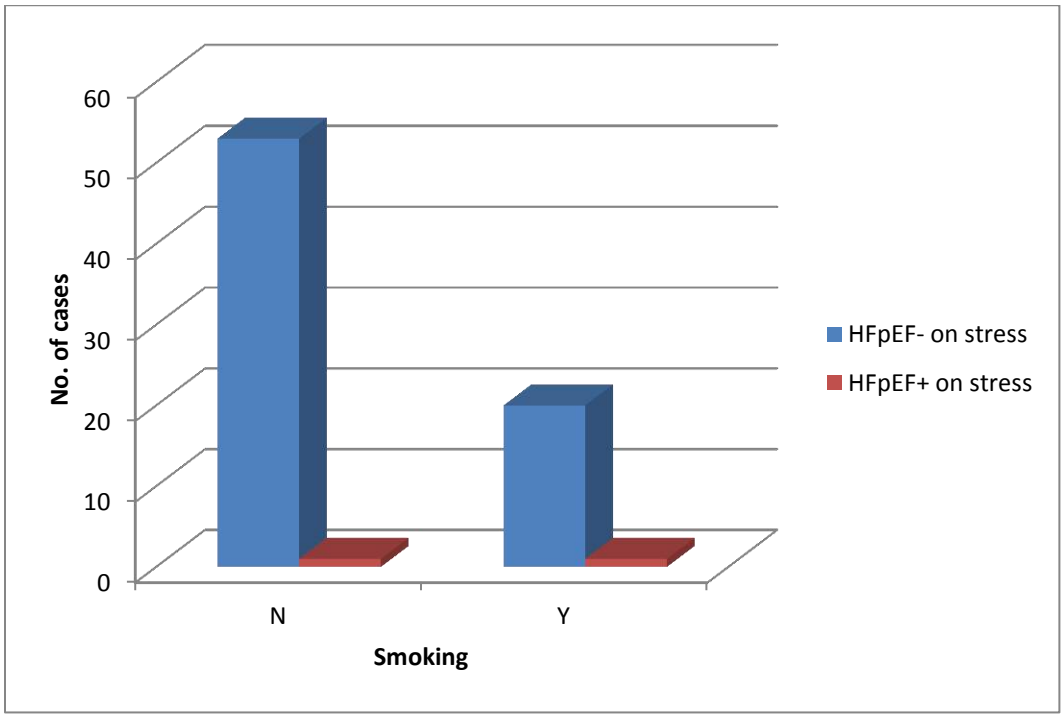

Figure 30- Distribution of smoking in group B

Table 22- Proteinuria distribution in group B

Proteinuria	HFpEF- on stress		HFpEF+ on stress		**Total**
N	51	70%	0	0%	51
Y	22	30%	2	100%	24
Total	73	100%	2	100%	75

Of the 2 cases to test HFpEF+ on stress, both had proteinuria. Of 73 cases to test HFpEF- on stress, 30% of cases had proteinuria.

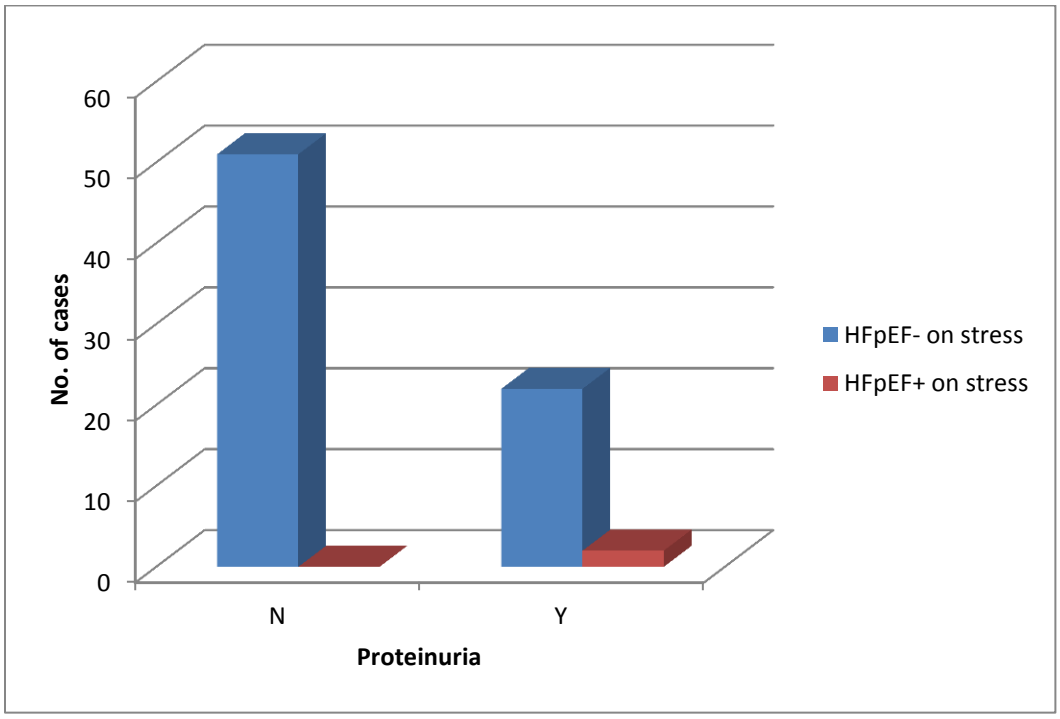

Figure 31- Proteinuria distribution in group B

Table 23- Glycosuria distribution in group B

Glycosuria	HFpEF- on stress		HFpEF+ on stress		**Total**
N	53	73%	1	50%	54
Y	20	27%	1	50%	21
Total	73	100%	2	100%	75

Of the 2 cases to test HFpEF+ on stress, 1 had glycosuria and 1 did not. Of 73 cases to test HFpEF- on stress, 27.4% of cases had glycosuria.

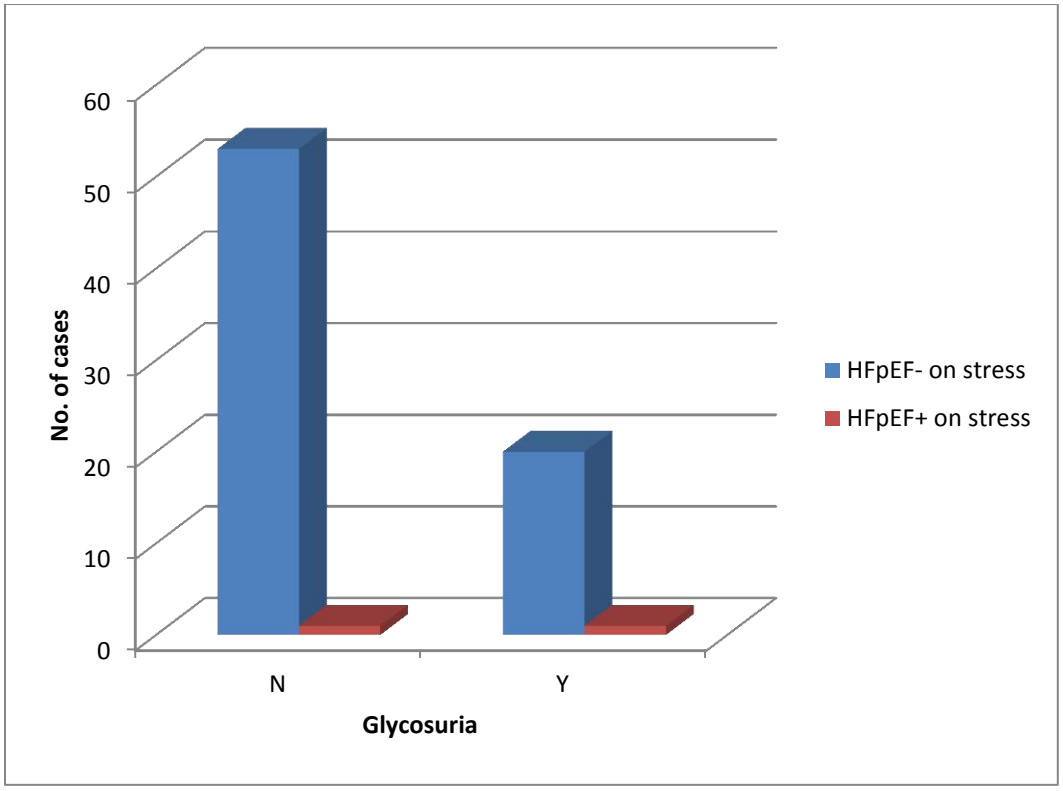

Figure 32- Glycosuria distribution in group B

Table 24- Distribution of vitals in group B

	HFpEF- on stress		HFpEF+ on stress	
	Mean	SD	Mean	SD
SBP (mm of Hg)	136.03	9.24	135.00	7.07
DBP (mm of Hg)	87.12	8.89	100.00	0.00
HR (/min)	76.63	4.01	76.00	11.31
Spo2% (in %)	98.16	1.55	99.00	0.00

In cases that tested HFpEF+ on stress, means of SBP, DBP, HR and Spo2% were 135.0, 100.0, 76 and 99. In cases that tested HFpEF- on stress, means of SBP, DBP, HR and Spo2% were 136.03, 87.12, 76.63 and 98.16 respectively.

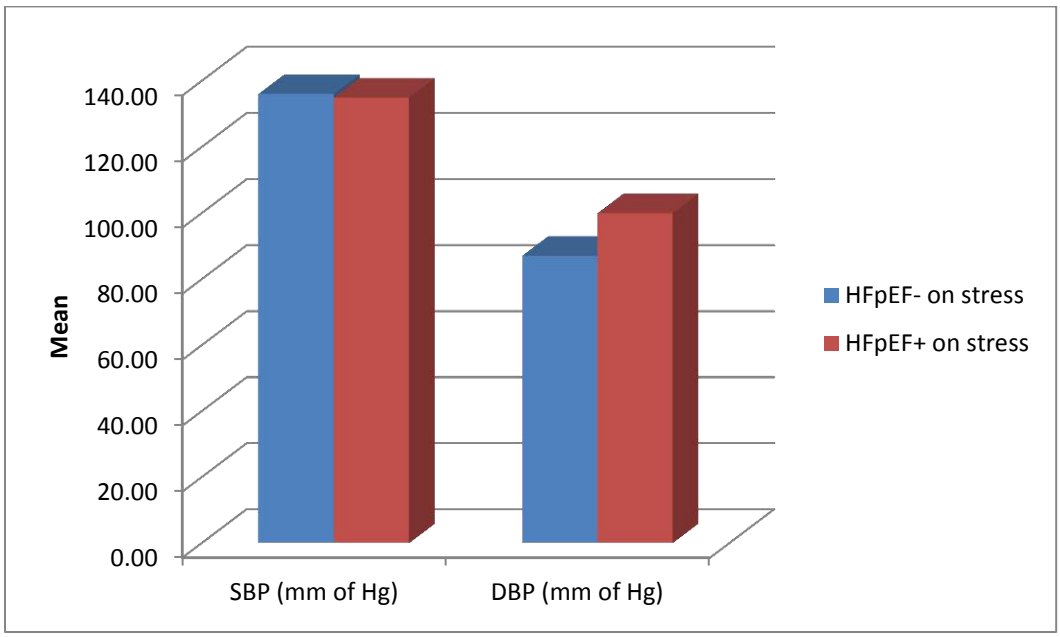

Figure 33- Distribution of blood pressure in group B

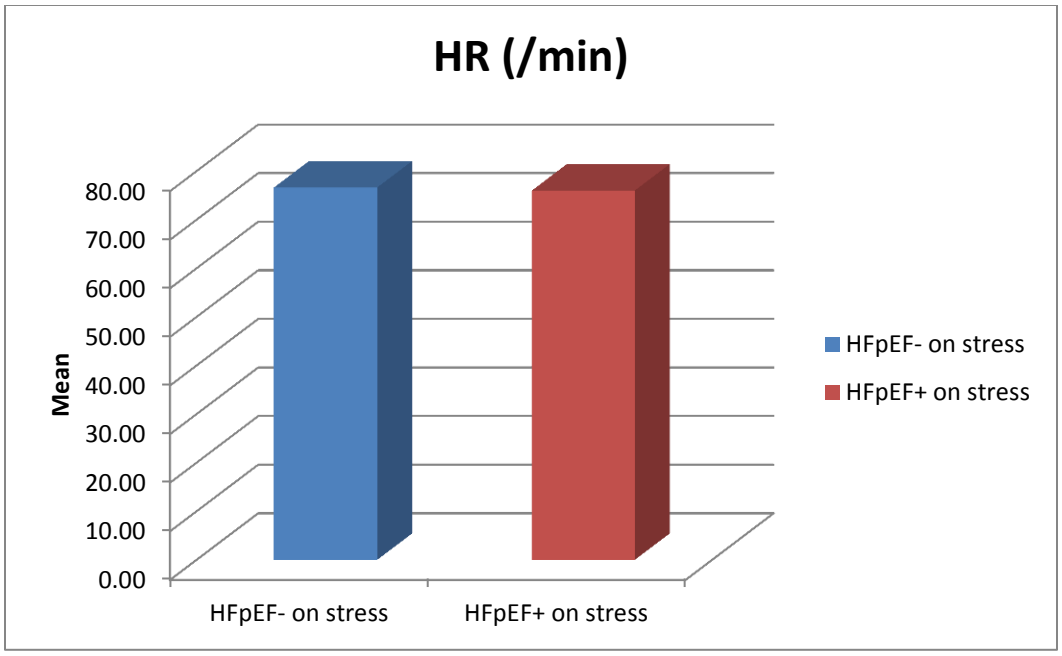

Figure 34- Distribution of HR in group B

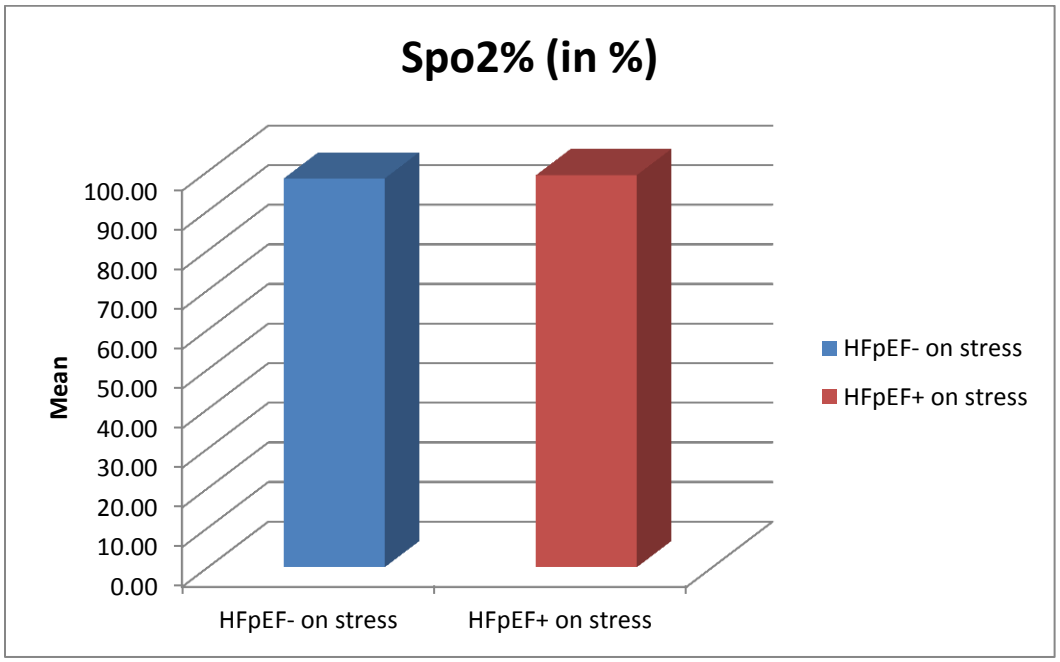

Figure 35- Distribution of Spo2% in group B

Table 25- Distribution of BMI in group B

	HFpEF- on stress		$HFpEF_+$ on stress	
BMI (kg/m2)	Mean 21.74	SD 3.10	Mean 22.12	SD 0.02

The 2 cases that tested HFpEF+ on stress had a mean BMI of 22.12 with SD 0.02 and cases that tested HFpEF- on stress had mean BMI of 21.74 with SD 3.10.

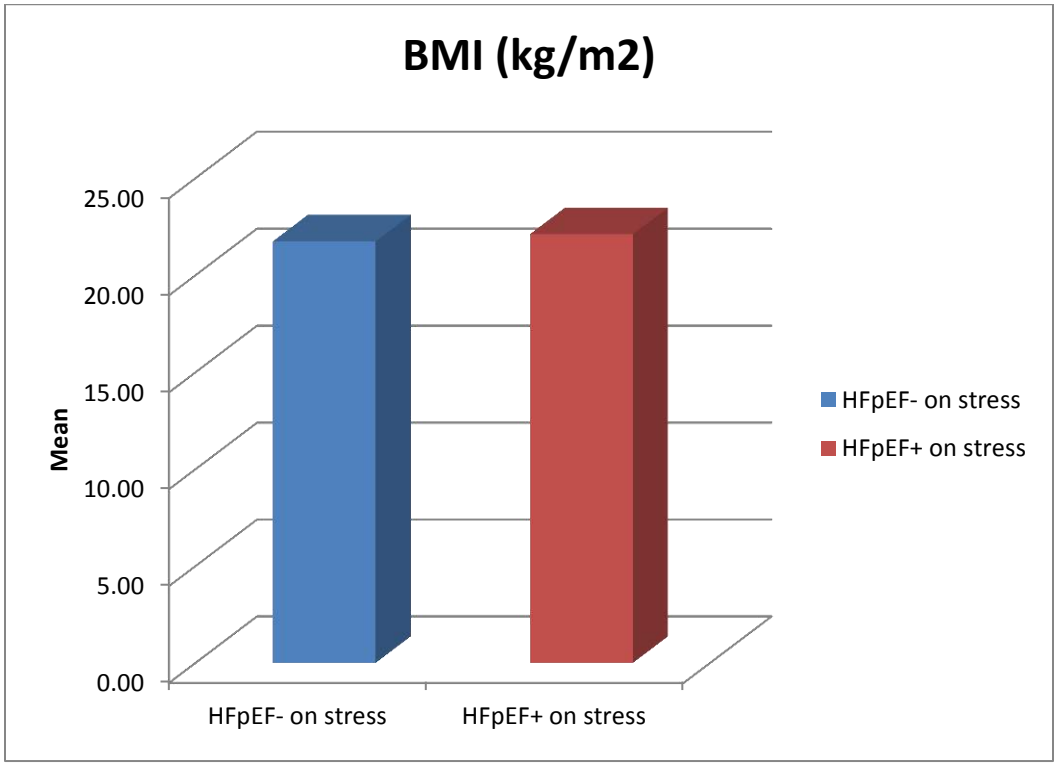

Figure 36- Distribution of BMI in group B

Table 26- Hemogram, RFT, albumin, RBS distribution in group A

	HFpEF- on stress		HFpEF+ on stress	
	Mean	SD	Mean	SD
Hb (g/dl)	12.50	1.95	9.75	0.35
TLC (/mm3)	8.14	7.16	5.45	0.35
RBS (mg/dl)	140.08	66.61	277.50	0.71
Urea (mg/dl)	29.15	9.27	21.00	8.49
Creatinine (mg/dl)	0.60	0.27	0.68	0.33
Sodium (mmol/l)	139.67	3.49	141.00	4.24
Potassium (mmol/l)	3.89	0.35	3.69	0.28
Albumin (g/dl)	3.65	0.39	2.95	0.49

With respect to Hb, it has a mean of 9.75 with SD .035 in HFpEF+ cases and a mean of 12.50 with SD 1.95 in HFpEF- cases. With respect to TLC, it has a mean of 5.45 with SD 0.35 in HFpEF+ cases and a mean of 8.14 with SD 7.16 in HFpEF- cases. With respect to RBS, it has a mean of 277.50 with SD 0.71 in HFpEF+ cases and a mean of 140.08 with SD 66.61 in HFpEF- cases. With respect to urea, it has a mean of 21 with SD 8.49 in HFpEF+ cases and a mean of 29.15 with SD 9.27 in HFpEF- cases. With respect to creatinine, it has a mean of 0.68 with SD 0.33 in HFpEF+ cases and a mean of 0.60 with SD 0.27 in HFpEF- cases. With respect to sodium, it has a mean of 141.0 with SD 4.24 in HFpEF+ cases and a mean of 139.67 with SD 3.49 in HFpEF- cases. With respect to potassium, it has a mean of 3.69 with SD 0.28 in HFpEF+ cases and a mean of 3.89 with SD 0.35 in HFpEF- cases. With respect to albumin, it has a mean of 2.95 with SD 0.49 in HFpEF+ cases and a mean of 3.65 with SD 0.39 in HFpEF- cases.

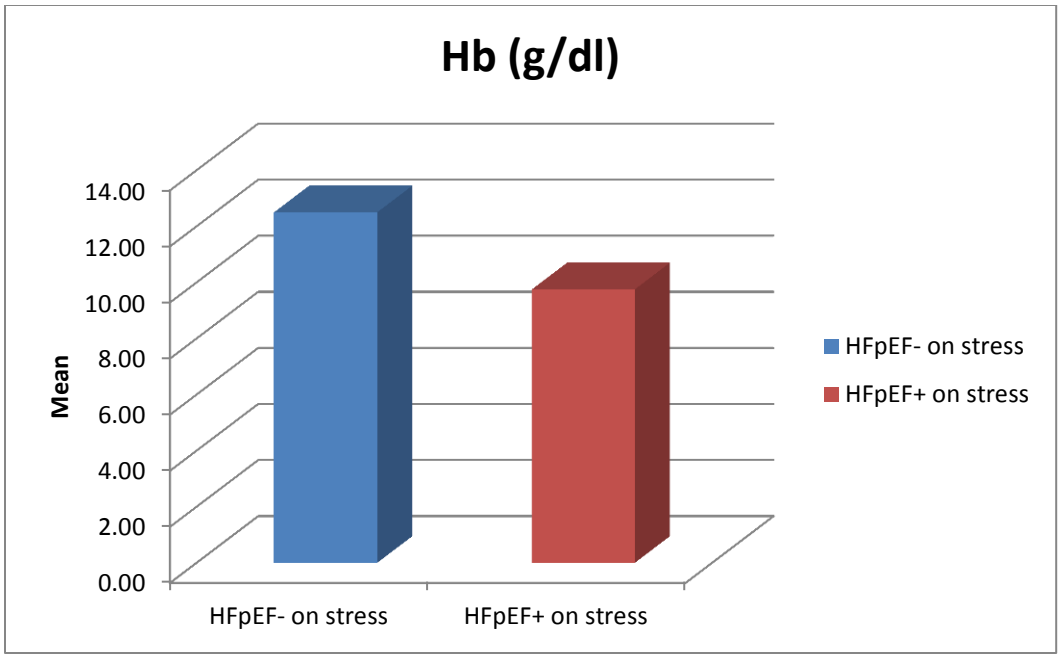

Figure 37- Distribution of Hb in group B

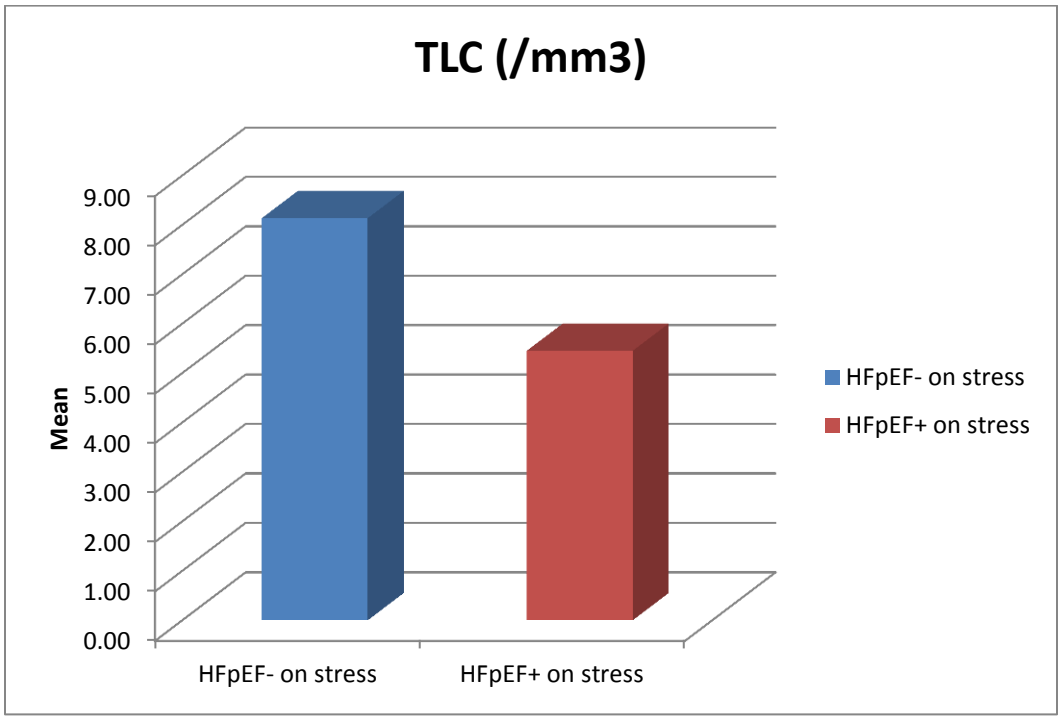

Figure 38- Distribution of TLC in group B

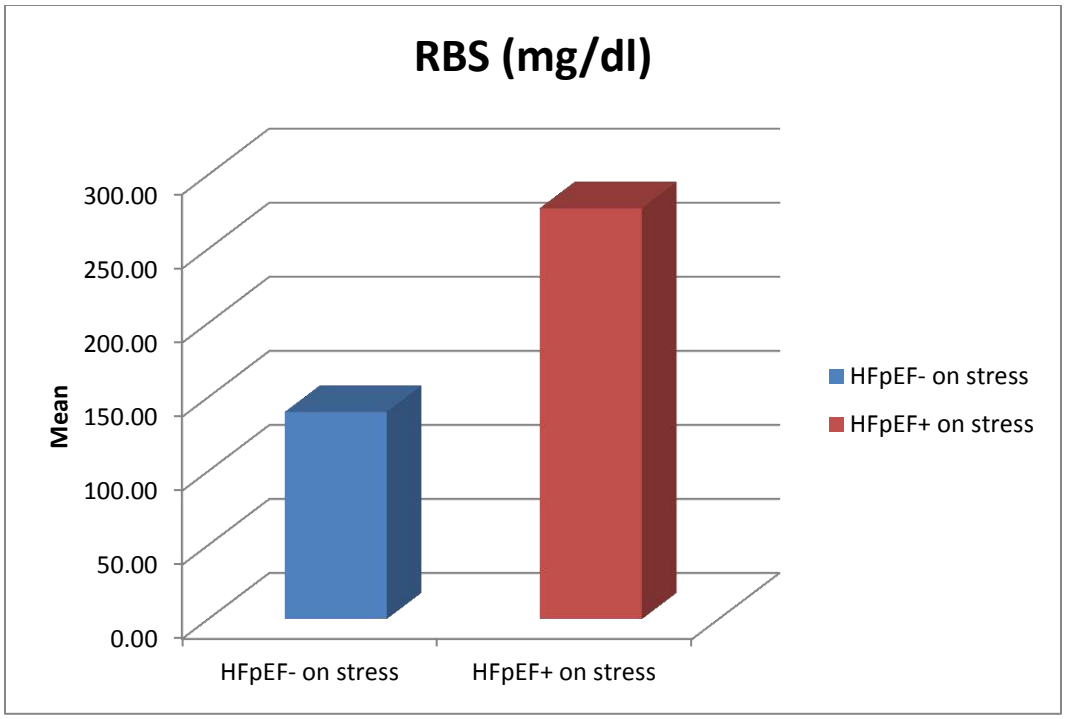

Figure 39- Distribution of RBS in group B

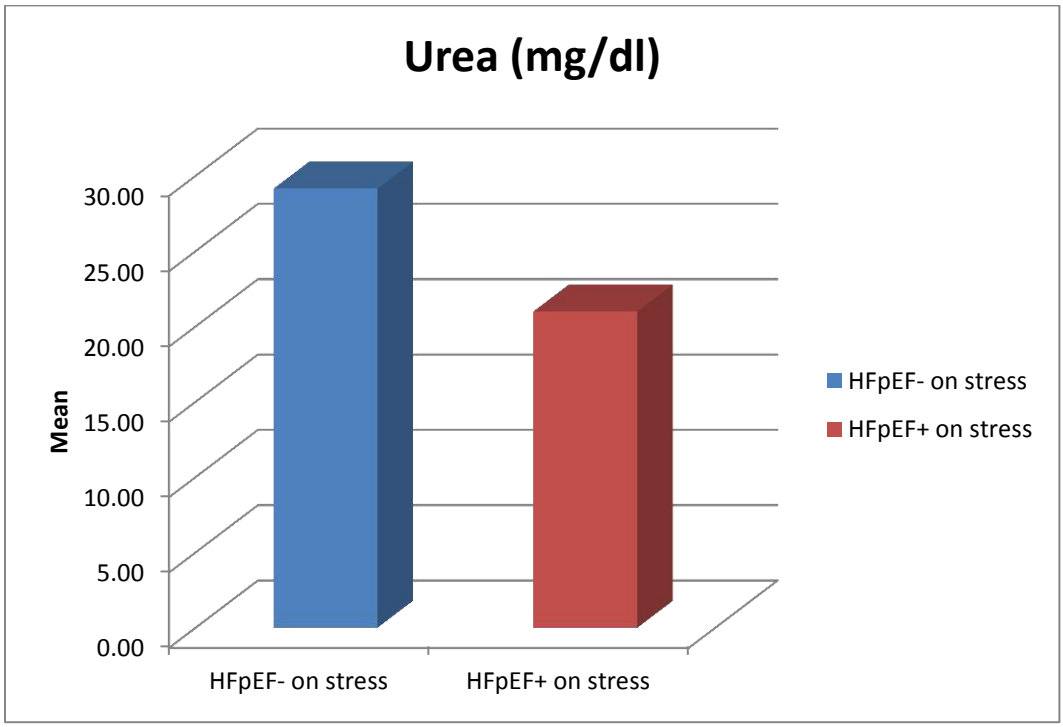

Figure 40- Distribution of urea in group B

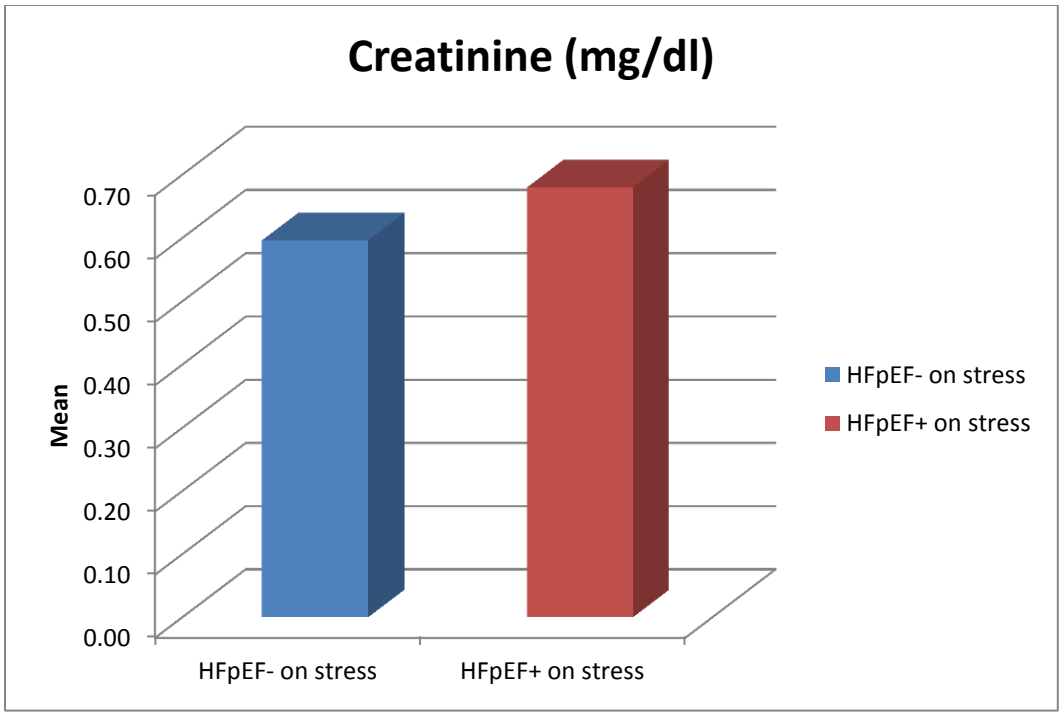

Figure 41- Distribution of creatinine in group B

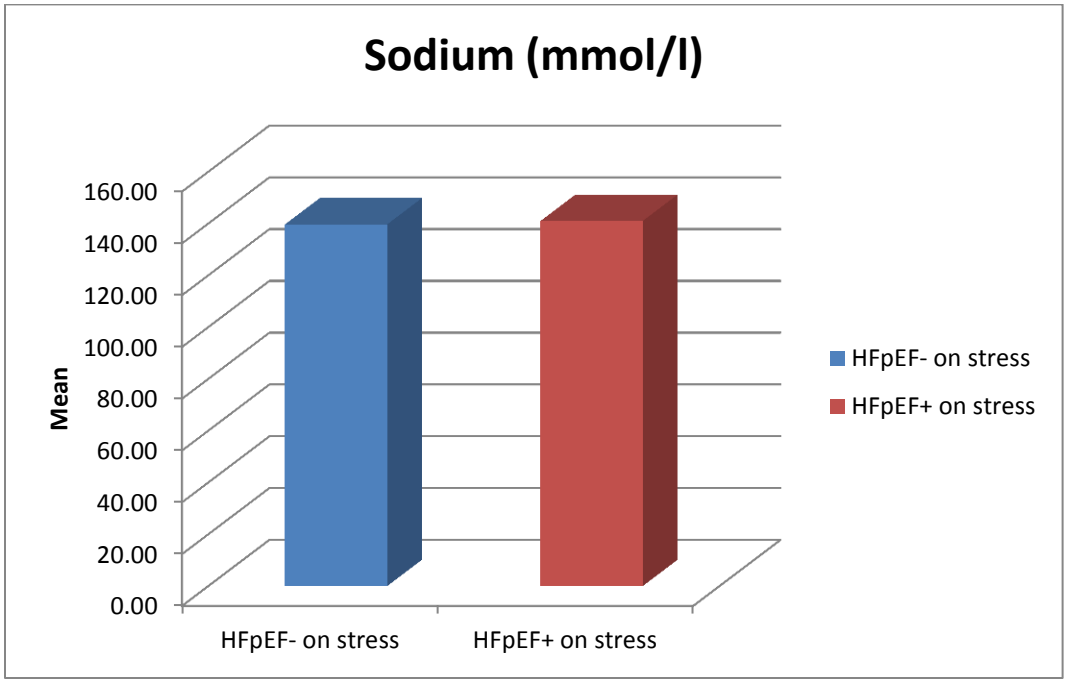

Figure 42- Distribution of sodium in group B

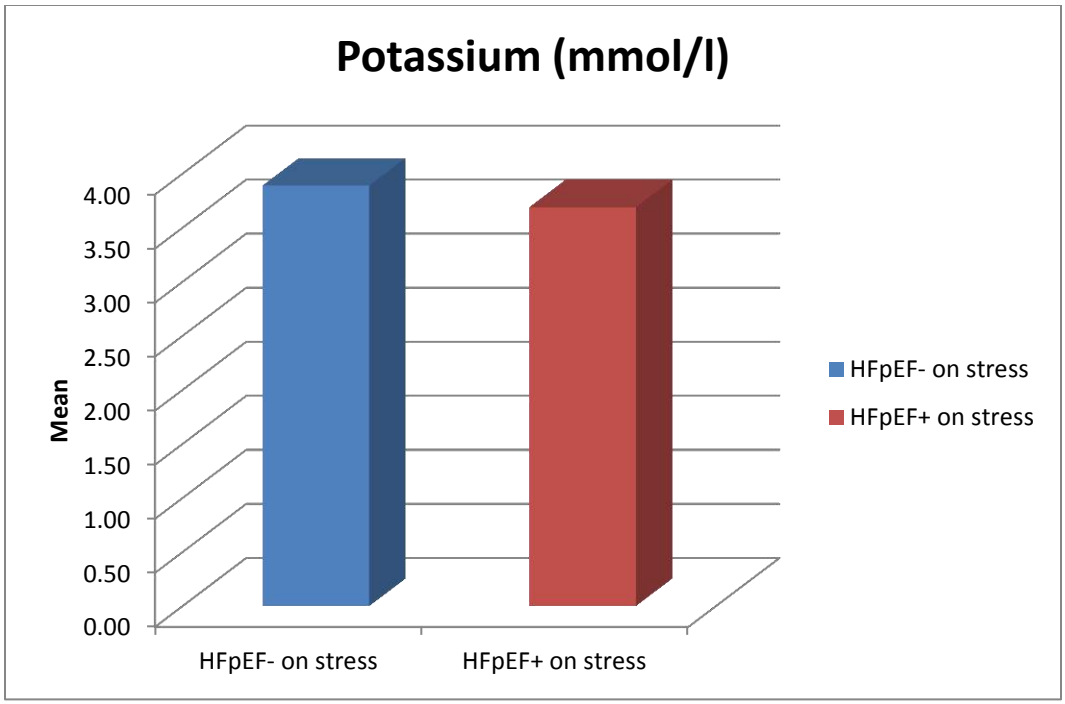

Figure 43- Distribution of potassium in group B

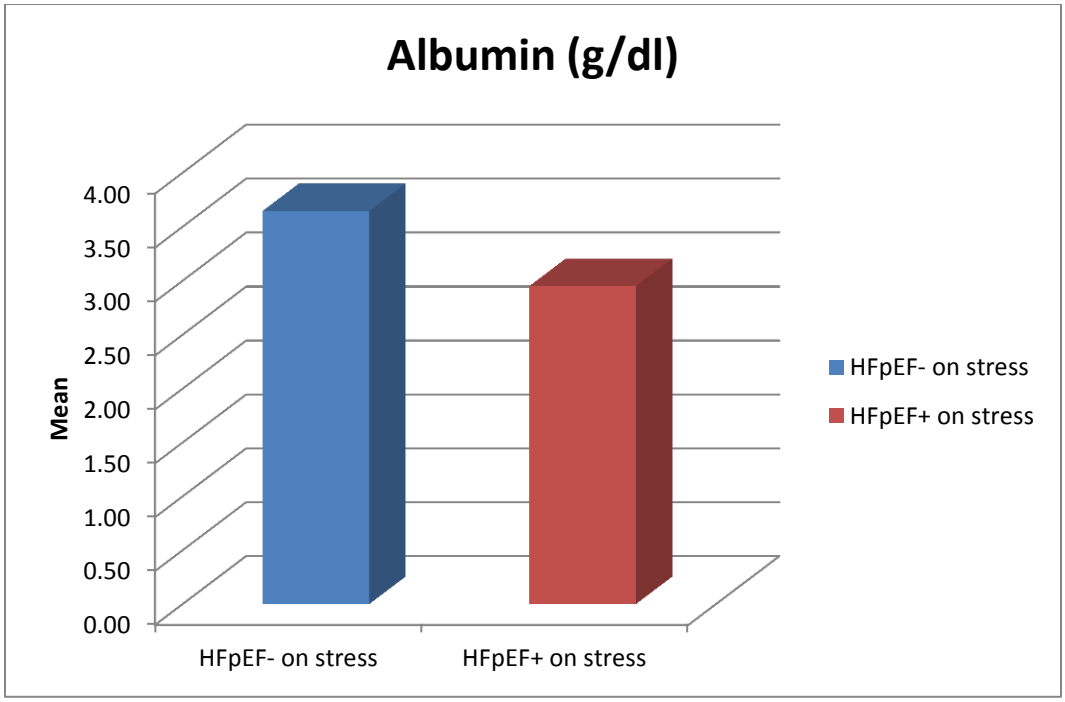

Figure 44-Distribution of albumin in group B

Table 27- Distribution of lipid profile in group B

	HFpEF- on stress		HFpEF+ on stress	
	Mean	SD	Mean	SD
Total Cholesterol (mg/dl)	184.37	46.65	204.50	21.92
TG (mg/dl)	176.95	46.57	147.50	24.75
HDL (mg/dl)	44.12	9.47	45.00	18.38
LDL (mg/dl)	102.19	31.91	132.50	79.90

With respect to total cholesterol, it has a mean of 204.50 with SD 21.92 in cases which tested HFpEF+ on stress and it has a mean of 184.37 with SD 46.65 in cases which tested HFpEF- on stress. With respect to TG, it has a mean of 147.50 with SD 24.75 in cases which tested HFpEF+ on stress and it has a mean of 176.95 with SD 46.57 in cases which tested HFpEF- on stress. With respect to LDL, it has a mean of 132.50 with SD 79.90 in cases which tested HFpEF+ on stress and it has a mean of 102.19 with SD 31.91 in cases which tested HFpEF- on stress. With respect to HDL, it has a mean of 45 with SD 18.38 in cases which tested HFpEF+ on stress and it has a mean of 44.12 with SD 9.47 in cases which tested HFpEF- on stress.

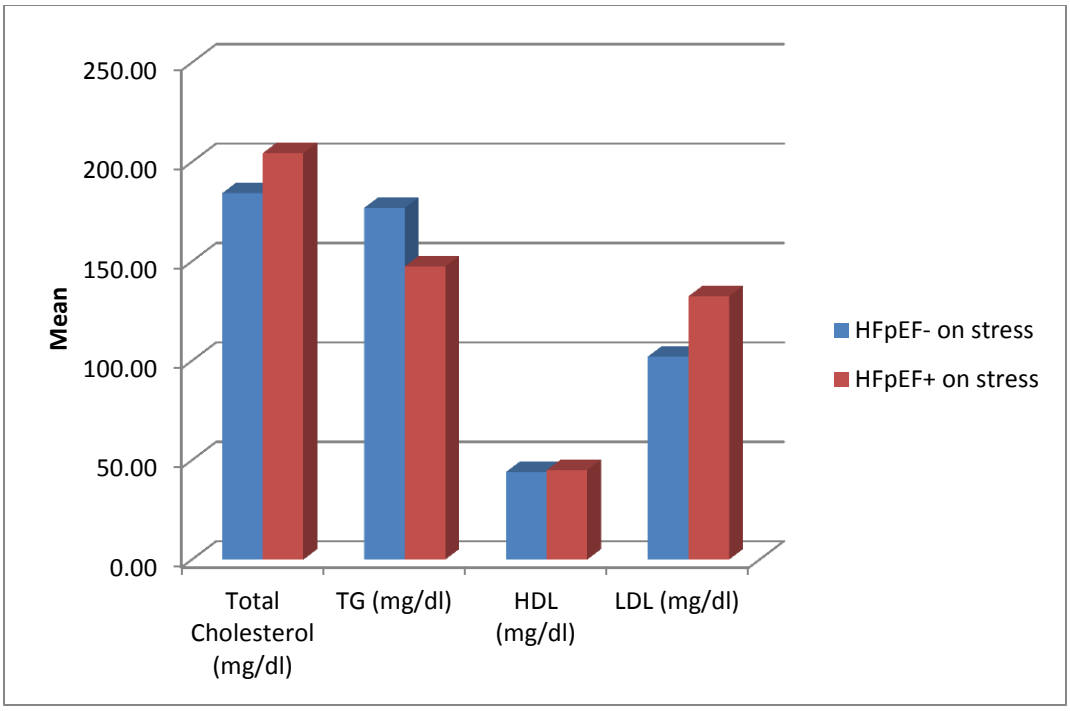

Figure 45- Distribution of lipid profile in group B

Table 28- Distribution of BNP in group B

	HFpEF- on stress		HFpEF+ on stress	
	Mean	SD	Mean	SD
BNP (pg/ml)	112.92	40.55	191.00	1.41

The 2 cases that tested HFpEF+ on stress had a mean BNP of 191 with SD 1.41 and cases that tested HFpEF- on stress had mean BNP of 112.92 with SD 40.55.

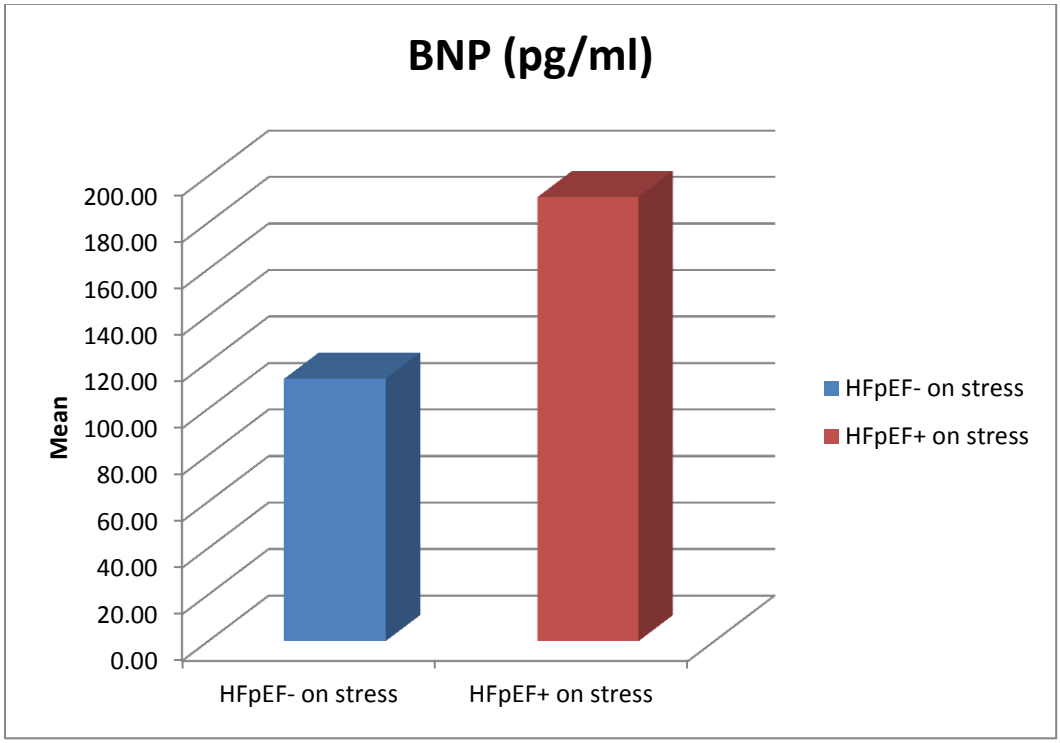

Figure 46- Distribution of BNP in group B

DISCUSSION

In this study, there were 150 cases- 75 cases of suspected HFpEF in group A and 75 cases of asymptomatic hypertension in group B. All cases underwent blood tests, ECG and urine routine analysis. Conventional echocardiography was then performed at rest. TMT was then performed according to Bruce protocol[44] and stress echocardiography was done during 1st minute of recovery. Comparisons were done within group A between 42 cases that tested HFpEF+ on stress and 33 cases that tested HFpEF- on stress with respect to blood and urine investigations, vitals, BMI, diabetic status, smoking and alcohol consumption.

Group A:

In group A, the mean age was 54.11±11.6 years and 65% were males. Out of 75 cases in this group, 42 tested HFpEF+ on stress which accounted to 56%. 33 cases or 44% tested HFpEF- on stress. In a study conducted by Belyavskiy E et al[26], 84.6% of the 13 patients with suspected HFpEF developed HFpEF during exercise.

In group A, of the 42 cases which tested HFpEF+ on stress, 73.8% were diabetic whereas for the 33 cases which tested HFpEF- on stress, only 18.2% were diabetic. This shows diabetes mellitus to be a statistically significant risk factor for abnormal DST echocardiography with p-value of 0.001. Diabetes mellitus is already a recognized risk factor for the development of HFpEF according to many previous studies.[3,6-12]

In group A, out of 18 cases with a history of smoking, 16 tested HFpEF+ on stress which means that 89.9% of smokers tested HFpEF+. 16 (38.1%) out of 42 cases which tested HFpEF+ on stress were smokers whereas only 2 (6.1%) out of 33 cases which tested HFpEF- on stress were smokers. This data shows that smoking is a statistically significant risk factor for abnormal DST echocardiography and eventually HFpEF as already shown in numerous studies.[3,6] This data is statistically significant with a p-value of 0.0001. Alcohol intake was however not statistically significant as a risk factor for abnormal DST echocardiography. Of the

cases that tested positive for HFpEF on stress, only 26.2% (11) had a history of alcohol consumption. Of the cases which tested HFpEF- on stress, 24.2% (8) consumed alcohol. This study shows that alcohol intake was statistically not significant with a p-value of 0.847.

Urine routine analysis in group A shows a correlation between presence of proteinuria and abnormal DST echocardiography. Out of 42 cases that tested HFpEF+ on stress, 25 cases or 59.5% had proteinuria, whereas out of 33 cases that tested HFpEF- on stress, only 3 cases or 9.1% had proteinuria. In group A, all the patients that had proteinuria were diabetic. Presence of proteinuria was a statistically significant factor for abnormal DST echocardiography with a p-value of 0.0001. Out of 37 diabetic cases in group A, 24 had glycosuria. Out of 42 cases that tested HFpEF+ on stress, 18 (42.9%) had glycosuria whereas out of 33 cases that tested HFpEF- on stress, only 6 (18.2%) had glycosuria. This shows that glycosuria is statistically significant with a p-value of 0.023.

With respect to the vitals in group A, the data showed that vitals such as heart rate, spo2, blood pressure had no correlation with outcome of DST echocardiography with p-values of 0.759, 0.536, 0.837 and 0.712 for SBP, DBP, heart rate and spo2%.

In group A, cases which tested HFpEF+ on stress had a mean BMI of 24.42 with SD of 3.19 and cases which tested HFpEF- on stress had a mean BMI of 22.44 with SD of 3.22. This data shows that BMI is a statistically important factor for abnormal DST echocardiography with a p-value of 0.010. Numerous studies[3,6-12] attribute obesity as a risk factor for developing HFpEF. In our study, cases of BMI 23-29.9 kg/m^2 were most prone to develop HFpEF. These include cases that were overweight (BMI=23-24.9 kg/m^2) and obesity grade 1 (BMI=25-29.9 kg/m^2) according to revised Indian guidelines.[45]

With respect to the lipid profile in group A, total cholesterol, TG and LDL were statistically significant factors for abnormal DST echocardiography. In group A, with respect to total cholesterol, it had a mean of 233.9 with

SD 41.41 in cases which tested HFpEF+ on stress and it had a mean of 168.0 with SD 43.03 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to TG, it has a mean of 209.38 with SD 43.98 in cases which tested HFpEF+ on stress and it has a mean of 151.82 with SD 27.48 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to LDL, it has a mean of 157.02 with SD 47.12 in cases which tested HFpEF+ on stress and it has a mean of 113.58 with SD 27.07 in cases which tested HFpEF- on stress. It has a p-value of 0.000. With respect to HDL, it has a mean of 45.55 with SD 15.42 in cases which tested HFpEF+ on stress and it has a mean of 43.76 with SD 8.36 in cases which tested HFpEF- on stress. It has a p-value of 0.550. HSL was statistically not significant.

In group A, various parameters of routine blood investigations were studied. With respect to Hb, it has a mean of 11.87 with SD 1.69 in HFpEF+ cases and a mean of 13.06 with SD 1.38 in HFpEF- cases with a p-value of 0.002. With respect to TLC, it has a mean of 7.33 with SD 1.64 in HFpEF+ cases and a mean of 7.23 with SD 1.44 in HFpEF- cases with a p-value of 0.783. With respect to RBS, it has a mean of 172.45 with SD 69.32 in HFpEF+ cases and a mean of 105.06 with SD 49.99 in HFpEF- cases with a p-value of 0.000. With respect to urea, it has a mean of 29.29 with SD 8.17 in HFpEF+ cases and a mean of 28.58 with SD 10.19 in HFpEF- cases with a p-value of 0.738. With respect to creatinine, it has a mean of 0.66 with SD 0.27 in HFpEF+ cases and a mean of 0.66 with SD 0.25 in HFpEF- cases with a p-value of 0.987. With respect to sodium, it has a mean of 143.5 with SD 3.1 in HFpEF+ cases and a mean of 137.24 with SD 4.7 in HFpEF- cases with a p-value of 0.000. With respect to potassium, it has a mean of 3.91 with SD 0.39 in HFpEF+ cases and a mean of 3.92 with SD 0.35 in HFpEF- cases with a p-value of 0.953. With respect to albumin, it has a mean of 3.28 with SD 0.34 in HFpEF+ cases and a mean of 3.87 with SD 0.4 in HFpEF- cases with a p-value of 0.000. BNP level was a statistically significant factor for the development of

HFpEF with a p-value of 0.000. BNP has a mean of 142.24 with SD 37.79 in 42 cases which tested HFpEF+ on stress and a mean of 81.12 with SD 23.64 in 33 cases which tested HFpEF- on stress.

On multivariate logistic regression analysis in group A involving diabetes mellitus, smoking, BMI and Hb. Diabetes mellitus was found to be the independent predictor of abnormal DST (OR=8.81, CI= 2.595- 29.902; p-value =0.000).

Group B:

In group B containing asymptomatic cases with hypertension, only 2 out of 75 cases tested HFpEF+ on stress, which amounts to only 2.7% of the total cases. In a study conducted by Belyavskiy E. et al,[26] a group of 19 asymptomatic cases with hypertension were studied and 0% of them developed HFpEF on stress.

Of the 2 cases in group B that tested HFpEF+ on stress, both were diabetic. Out of 73 cases that tested HFpEF- on stress, 48% had diabetes mellitus. Out of the 2 cases that tested HFpEF+ on stress, 1 had history of alcohol intake and 1 did not. Out of the 73 cases that tested HFpEF- on stress, 23% had history of alcohol intake. Out of the 2 cases that tested HFpEF+ on stress, 1 had history of smoking and 1 did not. Out of the 73 cases that tested HFpEF- on stress, 27% had history of smoking. Of the 2 cases to test HFpEF+ on stress, both had proteinuria. Of 73 cases to test HFpEF- on stress, 30% of cases had proteinuria. The 2 cases that tested HFpEF+ on stress had a mean BMI of 22.12 with SD 0.02 and cases that tested HFpEF- on stress had mean BMI of 21.74 with SD 3.10. The 2 cases that tested HFpEF+ on stress had a mean BNP of 191 with SD 1.41 and cases that tested HFpEF- on stress had mean BNP of 112.92 with SD 40.55.

SUMMARY AND CONCLUSION

- DST echo is a very useful tool in suspected HFpEF patients as 56% of them showed abnormal DST echo in our study.
- In asymptomatic patients with hypertension, only 2.67% of patients showed abnormal DST echo.
- In patients of suspected HFpEF, the cases which had abnormal DST echocardiography were predominantly diabetic, had a higher BMI, higher association with smoking, lower Hb and albumin, higher cholesterol, LDL, TG and higher BNP levels when compared to cases that had normal DST echocardiography.
- On multivariate logistic regression analysis of patients with suspected HFpEF involving diabetes mellitus, smoking, BMI and Hb. Diabetes mellitus was found to be the independent predictor of abnormal DST.

LIMITATIONS OF STUDY

1. Small sample size.
2. Single centered study.
3. There was no follow-up of patients. So, effectiveness of initiating early management and lifestyle modifications in patients on HFpEF could not be studies.
4. Echocardiographic measurements are time consuming and they may change in parameters if recorded later than 1-2 minutes after completion of TMT.

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S No.	MRD No.	Name	Age (years)	Sex	Symptomatic	Hypertension	Diabetes Mellitus	Alcohol intake	Smoking	BMI (kg/m2)	SBP (mm of Hg)	DBP (mm of Hg)	HR (/min)	Spo2% (in %)	Hb (g/dl)	TLC (/mm3)	RBS (mg/dl)	Urea (mg/dl)
1	8967	NS	44	M	Y	N	N	N	N	27.68	120	80	78	98	13.9	5.7	96	25
2	54439	PS	53	M	Y	N	N	N	N	22.42	120	80	68	99	12.2	9.7	87	35
3	98053	BS	67	M	Y	N	Y	Y	N	24.8	120	70	80	100	12.5	6.7	135	40
4	119380	VK	58	M	Y	N	Y	N	Y	26.1	110	70	82	95	10.2	4.9	187	15
5	123889	GS	72	M	Y	N	N	N	N	25.6	110	70	80	98	16	7.8	98	38
6	151104	GS	31	M	Y	N	N	N	Y	28.2	120	80	76	98	11.2	9.1	76	29
7	154857	RK	70	M	Y	N	N	Y	Y	21.65	120	70	84	96	11.3	8.9	102	18
8	157307	YJ	38	M	Y	N	N	N	N	20.19	110	80	72	99	11.9	7.9	89	37
9	159725	SS	50	F	Y	N	Y	N	N	24.6	110	70	72	98	14	4.9	209	19
10	185231	SK	64	M	Y	N	Y	N	N	23.21	110	70	74	99	13.4	8.7	187	28
11	199839	TL	49	M	Y	N	N	N	N	21.32	110	80	76	96	13.5	6.8	83	27
12	232806	DN	42	M	Y	N	Y	N	Y	20.42	110	70	73	100	12.2	5.8	193	37
13	247051	AG	54	M	Y	N	Y	N	N	21.22	120	70	78	98	12.3	9.8	81	19
14	309889	DS	69	M	Y	N	N	Y	N	24.12	110	70	80	100	14	4.9	76	29
15	402475	RA	47	M	Y	N	Y	N	Y	23.2	120	70	82	99	11.5	5.6	292	38
16	405463	LS	62	M	Y	N	N	Y	N	19.48	120	80	78	99	12.3	7.4	73	15
17	425560	AK	53	M	Y	N	Y	Y	Y	31.25	110	70	76	98	10.5	5	281	34
18	444991	NS	52	F	Y	N	N	Y	N	18.22	120	80	72	99	12.8	6.8	95	26
19	447783	CS	36	M	Y	N	Y	Y	N	24.91	120	70	74	95	13.7	7.9	186	28
20	451215	SK	78	M	Y	N	N	N	N	27.68	120	80	80	99	11	8	81	19
21	456275	BS	53	M	Y	N	N	Y	N	22.11	110	80	68	100	11.9	5.8	83	34
22	459533	BS	62	M	Y	N	Y	N	Y	26.88	120	80	80	95	13.5	6.8	92	32
23	482285	SK	60	M	Y	N	Y	N	Y	24.32	120	80	82	98	9.7	7.9	174	29
24	483841	DR	57	M	Y	N	Y	N	N	22.01	110	70	80	98	15.1	8.1	154	34
25	518022	RK	53	M	Y	N	N	Y	Y	19.81	130	80	76	96	14.4	9.2	94	24
26	618980	PK	60	M	Y	N	Y	N	Y	28.22	120	70	84	99	9.1	6.8	212	48
27	830302	MK	46	M	Y	N	Y	N	Y	29.44	110	70	72	98	10.5	7.4	173	29
28	834547	MK	64	F	Y	N	Y	N	N	20.54	110	80	72	99	8.2	8.9	299	37
29	842348	BL	63	M	Y	N	Y	N	N	24.55	120	80	74	100	13.3	8	278	18
30	868678	MK	55	F	Y	N	Y	N	N	26.44	120	80	76	100	10.8	4.9	191	28
31	911793	KL	49	M	Y	N	Y	N	N	21.3	120	80	73	98	14.5	6.8	218	49
32	914755	SS	56	M	Y	N	N	N	N	18.52	120	80	78	98	13.5	8.7	98	35
33	929566	HP	63	M	Y	N	Y	N	Y	25.88	120	80	80	99	10.4	8	191	28
34	940269	DG	30	M	Y	N	Y	N	Y	19.2	110	70	82	100	15.2	6.7	198	19
35	985667	BS	56	M	Y	N	Y	N	Y	22.7	120	80	78	95	9.5	6.4	287	35
36	1007818	MS	44	M	Y	N	N	Y	N	31.25	120	70	76	98	12.5	5.9	79	16
37	1008142	PK	56	F	Y	N	Y	N	N	23.57	110	70	72	98	11.4	6	254	24
38	1014841	BK	49	F	Y	N	N	N	N	24.91	120	70	74	96	12.6	8.9	103	26
39	1015273	RS	76	M	Y	N	N	Y	N	27.68	120	60	80	99	11.2	4.9	98	24
40	1016276	LC	51	F	Y	N	N	N	N	19.24	120	70	68	98	14.3	8.9	91	16

S No.	MRD No.	Creatinine (mg/dl)	Sodium (mmol/l)	Potassium (mmol/l)	Albumin (g/dl)	Total Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	BNP (pg/ml)	Proteinuria (Y/N)	Glycosuria (Y/N)	Echo EF (in %)	Diastolic failure in DST Echo (Y/N)
1	8967	0.85	141	3.96	4.2	214	129	41	161	54	N	N	60	N
2	54439	0.65	142	3.84	4.2	130	146	35	121	51	N	N	60	N
3	98053	0.59	136	3.46	3.8	146	167	38	140	79	N	Y	60	N
4	119380	0.98	146	3.19	3.2	265	189	39	181	189	Y	Y	60	Y
5	123889	1.01	135	4.06	4.5	134	143	48	141	59	N	N	55	N
6	151104	1.03	144	3.55	3.4	249	246	47	179	192	N	N	60	Y
7	154857	0.87	139	4.15	3.9	138	149	38	123	69	N	N	60	N
8	157307	0.54	136	4.13	3.7	213	179	35	100	97	N	N	60	N
9	159725	0.68	145	3.62	3.1	230	267	36	170	164	Y	Y	60	Y
10	185231	0.38	146	3.98	3.6	191	249	39	80	98	Y	Y	60	Y
11	199839	1.02	139	4.25	4.5	180	165	38	79	68	N	N	60	N
12	232806	1.08	147	3.99	3.1	231	223	37	143	159	Y	Y	55	Y
13	247051	0.21	145	3.56	3.8	180	213	41	79	134	N	Y	60	Y
14	309889	0.57	144	3.99	3.2	190	246	43	67	105	N	N	60	Y
15	402475	0.59	145	3.87	2.9	270	149	38	189	165	Y	N	60	Y
16	405463	0.21	139	3.49	4.2	161	115	41	90	69	N	N	60	N
17	425560	0.32	142	4.25	3.5	246	111	130	110	81	Y	N	60	Y
18	444991	0.62	137	4.36	4.3	134	127	35	130	51	N	N	60	N
19	447783	0.45	141	3.57	2.9	259	249	38	150	93	Y	Y	60	Y
20	451215	0.52	138	4.16	4.2	135	149	39	111	87	N	N	55	N
21	456275	0.15	147	3.49	3.7	197	279	37	144	92	N	N	60	Y
22	459533	0.59	140	3.67	3.6	234	232	42	181	138	Y	N	55	Y
23	482285	0.48	146	3.49	3.1	197	215	59	116	126	Y	N	60	Y
24	483841	1.05	139	3.79	3.8	162	189	57	101	95	N	Y	60	N
25	518022	0.56	144	3.89	2.7	276	256	49	172	109	N	N	60	Y
26	618980	0.84	141	4.59	3.1	197	218	46	132	107	Y	Y	60	Y
27	830302	0.98	143	4.15	2.9	231	197	59	212	96	Y	N	60	Y
28	834547	0.48	146	4.26	3.2	189	279	57	109	181	Y	Y	55	Y
29	842348	0.46	147	4.36	3.1	264	149	39	145	197	Y	N	60	Y
30	868678	0.79	138	3.56	3.5	295	219	37	107	82	N	N	60	Y
31	911793	0.49	149	3.89	2.9	221	134	49	181	162	N	Y	60	Y
32	914755	0.16	138	3.47	2.8	110	142	46	103	91	N	N	60	N
33	929566	0.17	144	3.59	3.9	217	159	43	142	73	Y	N	60	Y
34	940269	0.49	136	3.19	4.1	231	159	47	121	59	Y	Y	55	N
35	985667	0.64	145	3.19	2.8	217	149	46	192	97	Y	N	60	Y
36	1007818	0.28	134	3.46	4.2	164	164	43	102	67	N	N	60	N
37	1008142	1.04	146	3.95	3.3	297	179	38	250	137	Y	Y	60	Y
38	1014841	0.62	148	3.49	3.9	267	149	59	223	97	N	Y	60	Y
39	1015273	0.84	138	4.59	4.2	179	124	54	111	65	N	N	60	N
40	1016276	1.02	135	4.12	3.9	134	132	38	103	58	N	N	55	N

S No.	MRD No.	Name	Age (years)	Sex	Symptomatic	Hypertension	Diabetes Mellitus	Alcohol intake	Smoking	BMI (kg/m2)	SBP (mm of Hg)	DBP (mm of Hg)	HR (/min)	Spo2% (in %)	Hb (g/dl)	TLC (/mm3)	RBS (mg/dl)	Urea (mg/dl)
41	1019399	PK	40	F	Y	N	Y	N	N	25.44	110	80	80	99	13.4	5.9	121	34
42	1019771	NT	66	F	Y	N	N	N	N	26.4	110	80	82	96	11.9	9	91	25
43	1020495	GK	40	M	Y	N	N	N	N	19.44	120	70	80	100	13.5	7.9	86	16
44	1020879	SK	48	F	Y	N	N	N	N	18.62	120	80	76	98	12.5	5.7	108	34
45	1021115	SR	50	F	Y	N	N	N	N	21.23	110	80	84	100	13.7	4.9	92	25
46	1022284	RJ	44	F	Y	N	N	N	N	22.31	120	70	72	99	11.8	6.8	78	16
47	1022388	GS	33	M	Y	N	N	Y	N	21.3	110	70	72	99	13.9	8.9	76	34
48	1022652	JA	40	F	Y	N	N	N	N	21.6	110	70	74	98	12.5	4.8	79	48
49	1027107	KS	49	M	Y	N	N	Y	N	22.5	120	70	76	99	13.7	8.7	72	29
50	1035721	NP	60	M	Y	N	Y	N	N	23.41	120	80	73	95	12.5	9.8	109	37
51	1036351	AJ	56	M	Y	N	Y	N	Y	24.3	110	80	78	99	8.4	5	199	18
52	1062902	AJ	71	M	Y	N	Y	Y	Y	20.23	120	80	80	100	12.9	6.8	180	28
53	1065113	NM	60	F	Y	N	Y	N	N	20.44	110	70	82	95	15.8	7.9	98	49
54	1080496	RG	45	M	Y	N	Y	Y	N	21.35	120	80	78	98	14.5	9.1	154	35
55	1084519	HL	40	M	Y	N	N	N	N	25.36	120	80	76	98	13.4	8.3	79	28
56	1085271	BS	37	M	Y	N	N	Y	N	22.1	120	70	72	96	11.8	7.6	71	19
57	1085310	PK	57	F	Y	N	N	N	N	23.5	120	80	74	99	12.5	4.9	73	35
58	1086567	SG	75	F	Y	N	Y	N	N	26.65	120	70	80	98	11.9	7.5	187	16
59	1098896	SK	52	F	Y	N	N	N	N	24.6	120	80	80	100	13.4	8.7	107	24
60	1113409	MS	52	M	Y	N	Y	Y	Y	24.25	110	80	78	95	10.5	5	208	26
61	1115235	NV	60	F	Y	N	N	N	N	19.8	120	70	79	98	13.6	9.6	98	24
62	1118942	NA	61	F	Y	N	N	N	N	19.2	110	70	68	98	12.1	6	118	16
63	1120523	GK	52	F	Y	N	Y	N	N	29.48	120	70	80	96	10.1	8.7	190	34
64	1123001	P	44	F	Y	N	Y	N	N	31.25	120	80	82	99	11.2	8	192	42
65	1123015	JS	50	F	Y	N	N	N	N	18.22	120	80	80	98	13.3	8.3	90	32
66	1123962	IS	45	M	Y	N	N	N	N	24.91	130	80	76	99	10.8	8.9	78	17
67	1124143	AK	64	M	Y	N	N	N	N	27.68	130	80	84	96	14.5	6	104	40
68	1212499	RA	62	F	Y	N	Y	Y	N	19.22	120	80	72	100	10.5	5.7	228	42
69	1213748	AP	42	M	Y	N	Y	Y	Y	28.2	120	80	72	98	11.4	9.7	278	18
70	1213749	BK	57	F	Y	N	N	N	N	20.55	110	80	74	100	15.2	6.7	116	37
71	1215768	SR	47	F	Y	N	N	N	N	24.36	120	80	76	99	11.5	4.9	92	28
72	1217158	SC	70	M	Y	N	Y	N	N	22.1	120	70	73	99	12.5	7.8	345	19
73	1217520	KK	72	M	Y	N	Y	N	N	23.14	120	80	78	98	12.4	9.1	165	35
74	1217812	CK	57	F	Y	N	Y	N	N	26.55	120	80	80	99	12.6	8.9	198	28
75	121886	AK	68	M	Y	N	N	N	N	21.54	140	90	82	95	11.2	7.9	76	44
76	121897	AR	64	M	N	Y	N	N	Y	19.8	130	90	78	99	10.3	4.9	79	43
77	122002	SL	67	M	N	Y	Y	N	Y	16.54	150	90	76	100	13.4	8.7	156	19
78	146315	SR	60	F	N	Y	Y	N	N	19.8	140	100	72	95	11.9	6.8	178	38
79	160374	RK	55	M	N	Y	N	N	N	22.54	130	80	74	98	13.5	5.8	99	28
80	162249	RA	46	M	N	Y	Y	Y	Y	22.65	130	90	80	98	12.5	9.8	105	49

S No.	MRD No.	Creatinine (mg/dl)	Sodium (mmol/l)	Potassium (mmol/l)	Albumin (g/dl)	Total Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	BNP (pg/ml)	Proteinuria (Y/N)	Glycosuria (Y/N)	Echo EF (in %)	Diastolic failure in DST Echo (Y/N)
41	1019399	0.91	139	4.36	2.8	197	134	47	130	196	N	Y	60	Y
42	1019771	0.65	142	3.65	2.9	194	279	46	125	137	N	N	60	Y
43	1020495	0.49	138	3.89	3.7	219	194	49	168	102	N	N	60	N
44	1020879	1.04	139	3.79	3.4	297	219	48	149	167	N	N	60	Y
45	1021115	0.63	144	3.97	4.2	153	179	43	101	98	N	N	60	N
46	1022284	0.45	145	4.56	3.8	110	146	39	67	93	N	N	60	N
47	1022388	0.6	128	4.12	3.9	197	116	49	101	76	N	N	55	N
48	1022652	0.94	129	4.13	4.1	161	179	59	92	94	N	N	60	N
49	1027107	0.74	137	4.02	3.6	95	197	38	68	140	N	N	60	Y
50	1035721	0.59	128	4.01	3.6	294	164	59	143	92	Y	Y	60	N
51	1036351	0.65	139	3.88	3.8	267	246	57	102	173	Y	N	60	Y
52	1062902	0.48	144	4.98	3.9	210	226	51	168	151	Y	N	55	Y
53	1065113	0.61	143	4	3.8	110	179	53	68	67	Y	Y	60	N
54	1080496	0.21	142	4.16	3.3	279	179	38	208	176	Y	Y	60	Y
55	1084519	0.95	144	4.11	3.4	195	234	34	101	98	N	N	60	Y
56	1085271	0.84	132	4.03	3.8	179	159	38	98	91	N	N	60	N
57	1085310	0.15	131	3.65	3.5	137	94	49	67	73	N	N	55	N
58	1086567	0.62	146	3.98	3.2	271	198	43	140	182	Y	Y	60	Y
59	1098896	0.64	138	3.49	3.4	219	148	49	138	61	N	N	60	N
60	1113409	0.58	142	3.79	3.8	279	219	38	214	157	Y	Y	60	Y
61	1115235	1.03	143	4.06	2.8	199	234	32	141	137	N	N	60	Y
62	1118942	0.7	129	4.2	3.9	120	189	45	98	98	N	N	60	N
63	1120523	0.24	147	3.84	3.5	290	180	38	240	190	Y	Y	60	Y
64	1123001	0.91	145	4.9	3.1	230	222	32	180	168	N	Y	60	Y
65	1123015	0.59	142	4	3.6	224	116	47	167	100	N	N	60	N
66	1123962	0.9	147	4.15	3.3	280	140	48	221	127	N	N	60	Y
67	1124143	0.81	142	3.9	4	198	110	21	101	80	N	N	55	N
68	1212499	0.85	144	3.96	3.2	214	214	39	161	199	Y	N	60	Y
69	1213748	0.65	142	3.84	3	230	230	35	191	173	Y	Y	60	Y
70	1213749	0.59	144	3.46	3.8	146	146	38	140	92	N	N	60	N
71	1215768	0.98	134	3.19	3.6	165	165	39	121	85	N	N	60	N
72	1217158	1.01	139	4.06	2.7	134	134	37	141	77	N	Y	60	N
73	1217520	1.03	137	3.55	3.4	249	249	42	179	149	N	N	60	Y
74	1217812	0.87	139	4.15	2.9	238	238	59	223	180	Y	N	60	Y
75	121886	0.54	141	4.13	3.7	213	213	57	100	179	N	N	60	N
76	121897	0.68	143	3.62	3.5	130	130	49	91	92	Y	Y	60	N
77	122002	0.38	135	3.98	3.9	191	191	46	80	165	N	Y	55	N
78	146315	1.02	147	4.25	3.5	180	180	59	79	69	Y	Y	60	N
79	160374	1.08	139	3.99	4.1	231	231	57	91	94	N	N	60	N
80	162249	0.21	138	3.56	3.8	180	180	39	79	82	Y	Y	60	N

S No.	MRD No.	Name	Age (years)	Sex	Symptomatic	Hypertension	Diabetes Mellitus	Alcohol intake	Smoking	BMI (kg/m2)	SBP (mm of Hg)	DBP (mm of Hg)	HR (/min)	Spo2% (in %)	Hb (g/dl)	TLC (/mm3)	RBS (mg/dl)	Urea (mg/dl)
81	164050	UR	75	F	N	Y	N	N	N	21.36	120	70	68	96	13.7	4.9	94	28
82	164560	SK	65	M	N	Y	Y	N	Y	24.5	130	90	80	99	11.8	5.6	166	15
83	165097	GS	67	M	N	Y	N	Y	N	22.36	140	80	82	98	13.9	7.4	97	35
84	170699	PK	55	M	N	Y	Y	Y	N	24.56	140	90	80	99	15.1	5	157	25
85	191248	MK	68	F	N	Y	Y	N	Y	24.33	130	90	76	96	9.5	6.8	168	16
86	225257	BP	52	M	N	Y	Y	N	N	19.8	130	90	84	100	14.3	7.9	219	35
87	226105	TS	61	M	N	Y	N	Y	N	16.89	120	80	72	98	14.9	8	92	40
88	229100	JT	63	M	N	Y	Y	N	Y	22.31	130	100	72	100	8.8	5.8	213	15
89	253803	SA	63	F	N	Y	N	N	N	24.32	140	80	74	99	11.9	6.8	94	38
90	341424	RK	57	M	N	Y	N	N	N	26.5	140	80	76	99	13.4	7.9	87	29
91	352646	KS	59	M	N	Y	Y	Y	N	23.4	150	90	73	98	16	8.1	167	18
92	354673	SK	58	M	N	Y	Y	N	N	27.68	120	80	78	99	12.4	9.2	125	37
93	377757	NK	62	M	N	Y	N	Y	N	22.42	140	90	80	95	8.3	6.8	119	19
94	432175	KK	63	M	N	Y	N	Y	N	24.8	130	90	82	99	13	7.4	96	28
95	478538	SD	65	F	N	Y	Y	N	N	20.23	150	110	78	100	9.5	8.9	376	27
96	479419	AS	61	M	N	Y	Y	N	Y	25.6	140	100	76	95	10	8	214	37
97	536663	VC	67	M	N	Y	Y	N	Y	18.2	130	90	72	98	8.6	4.9	267	19
98	568529	HP	60	M	N	Y	N	N	N	21.65	130	80	74	98	11.8	6.8	89	29
99	613422	AS	51	M	N	Y	N	Y	N	20.19	140	90	80	96	14	8.7	78	38
100	620458	SV	65	F	N	Y	N	N	N	19.22	130	80	68	99	12.6	8	97	15
101	630518	RS	67	M	N	Y	N	N	Y	23.21	140	90	80	98	11.5	6.7	76	34
102	643385	AR	54	M	N	Y	N	N	Y	21.32	140	100	82	99	11	6.4	82	26
103	644622	SK	62	F	N	Y	Y	N	N	20.42	140	100	80	96	9.8	5.9	197	28
104	648483	VK	67	M	N	Y	N	Y	Y	21.22	150	90	76	100	14.6	6	93	19
105	653581	JP	74	M	N	Y	N	N	Y	19.82	150	90	84	98	13.5	8.9	73	23
106	656621	RG	72	M	N	Y	N	N	Y	22.6	140	90	72	100	10.1	4.9	112	16
107	784493	BR	73	F	N	Y	Y	N	N	22.5	140	90	72	99	13.4	8.9	178	42
108	857197	PR	65	F	N	Y	Y	N	N	19.8	150	90	74	99	12.5	5.9	184	32
109	916749	MS	75	M	N	Y	N	N	N	18.8	140	80	76	98	14	9	90	17
110	982928	SS	51	M	N	Y	Y	Y	N	17.56	120	80	73	99	13.5	8.7	167	40
111	985516	SK	68	M	N	Y	N	N	N	17.56	140	90	78	95	15	9.7	80	42
112	992983	MS	71	M	N	Y	N	Y	N	26.56	110	70	80	99	12.6	5.9	88	18
113	1006407	GK	56	F	N	Y	Y	N	N	27.68	150	110	82	100	9.9	5.9	270	37
114	1011855	PK	73	M	N	Y	Y	N	Y	22.42	130	90	78	95	10.2	6.7	190	28
115	1013714	SK	55	M	N	Y	Y	N	N	24.8	140	80	76	98	12.5	8.7	235	19
116	1014919	DP	40	M	N	Y	Y	N	Y	20.23	140	100	72	98	9.2	7.9	291	35
117	1015142	PK	53	F	N	Y	N	N	N	25.6	130	90	74	96	16	8.7	97	28
118	1016613	JK	55	M	N	Y	N	N	N	18.2	140	80	80	99	15.2	6.1	78	44
119	1018737	KS	53	M	N	Y	Y	N	N	21.65	150	90	68	98	11.3	7.3	248	43
120	1019154	BK	45	F	N	Y	Y	N	N	20.19	140	100	80	99	8.9	9.1	221	19

S No.	MRD No.	Creatinine (mg/dl)	Sodium (mmol/l)	Potassium (mmol/l)	Albumin (g/dl)	Total Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	BNP (pg/ml)	Proteinuria (Y/N)	Glycosuria (Y/N)	Echo EF (in %)	Diastolic failure in DST Echo (Y/N)
81	164050	0.57	138	3.99	4.2	190	190	37	67	73	N	N	60	N
82	164560	0.59	138	3.87	2.9	170	170	49	89	178	Y	N	60	N
83	165097	0.21	141	3.49	4.2	161	161	46	90	98	N	N	60	N
84	170699	0.32	142	4.25	3.5	146	146	43	110	96	N	Y	55	N
85	191248	0.62	146	4.36	3.3	134	134	47	130	94	Y	N	60	N
86	225257	0.45	140	3.57	3.9	159	159	46	94	151	N	N	60	N
87	226105	0.52	135	4.16	4.2	135	135	43	111	67	N	N	60	N
88	229100	0.15	144	3.49	3.7	197	197	38	200	176	Y	Y	60	N
89	253803	0.59	139	3.67	3.6	134	134	59	81	98	N	N	60	N
90	341424	0.48	136	3.49	3.8	197	197	54	116	91	N	N	60	N
91	352646	1.05	135	3.79	3.8	162	162	38	101	73	N	Y	60	N
92	354673	0.56	138	3.89	3.9	176	176	47	72	82	N	N	60	N
93	377757	0.84	139	4.59	3.1	197	197	46	132	61	Y	N	60	N
94	432175	0.98	137	4.15	3.9	231	231	49	212	157	N	N	60	N
95	478538	0.48	145	4.26	2.9	189	189	48	109	137	Y	N	60	N
96	479419	0.46	141	4.36	2.9	164	164	43	92	98	Y	N	60	N
97	536663	0.79	145	3.56	3.8	295	295	39	107	190	Y	Y	60	N
98	568529	0.49	139	3.89	4	121	121	49	81	168	N	N	60	N
99	613422	0.16	142	3.47	3.6	110	110	59	103	100	N	N	60	N
100	620458	0.17	137	3.59	3.9	117	117	38	72	127	N	N	60	N
101	630518	0.49	141	3.19	4	231	231	59	121	80	N	N	55	N
102	643385	0.64	138	3.96	3.2	117	117	57	92	99	N	N	60	N
103	644622	0.28	137	3.84	3.1	190	164	51	102	173	Y	N	60	N
104	648483	1.04	140	3.46	3.8	264	97	53	180	92	N	N	60	N
105	653581	0.62	136	3.19	3.8	189	167	38	120	85	N	N	60	N
106	656621	0.84	139	4.06	3.5	195	179	34	130	77	Y	N	60	N
107	784493	1.02	138	3.55	3.4	167	134	38	131	149	Y	Y	60	N
108	857197	0.25	141	4.15	3.9	159	197	49	110	130	N	Y	60	N
109	916749	0.49	137	4.13	3.7	165	94	43	98	110	N	N	60	N
110	982928	0.16	146	3.62	3.5	231	219	49	130	130	Y	Y	60	N
111	985516	0.64	137	3.98	3.9	179	297	38	89	96	N	N	60	N
112	992983	0.84	138	4.25	4.5	140	153	32	91	68	N	N	55	N
113	1006407	0.48	149	3.99	3.1	197	110	45	119	159	Y	N	60	N
114	1011855	0.61	138	3.56	3.6	194	197	38	152	67	N	Y	60	N
115	1013714	0.78	144	3.99	4.2	219	161	32	120	58	N	N	60	N
116	1014919	0.89	146	3.87	2.9	297	95	47	143	61	Y	N	60	N
117	1015142	0.15	135	3.49	4.2	153	294	48	103	90	N	N	60	N
118	1016613	0.56	134	4.25	3.5	110	267	21	69	178	N	N	60	N
119	1018737	0.48	136	4.36	2.8	197	210	59	110	160	Y	Y	60	N
120	1019154	1.08	138	3.57	3.4	161	110	54	94	184	Y	Y	60	N

S No.	MRD No.	Name	Age (years)	Sex	Symptomatic	Hypertension	Diabetes Mellitus	Alcohol intake	Smoking	BMI (kg/m2)	SBP (mm of Hg)	DBP (mm of Hg)	HR (/min)	Spo2% (in %)	Hb (g/dl)	TLC (/mm3)	RBS (mg/dl)	Urea (mg/dl)
121	1019158	NK	62	F	N	Y	Y	N	N	19.22	140	80	82	96	14	8.2	196	38
122	1020407	SD	54	F	N	Y	N	N	N	23.21	130	80	80	100	13.4	4.8	79	28
123	1020440	GK	51	F	N	Y	N	N	N	21.32	130	80	76	98	13.5	8.2	88	49
124	1023014	AK	50	F	N	Y	Y	N	N	20.42	140	80	84	100	12.2	9.1	91	28
125	1024244	HS	60	M	N	Y	N	Y	N	21.22	130	80	72	99	12.3	5.7	99	15
126	1025634	HK	48	F	N	Y	N	N	N	19.82	130	80	72	99	14	9.8	94	35
127	1028453	RK	53	F	N	Y	Y	N	N	19.2	140	100	74	98	11.5	10	246	25
128	1033230	GK	68	F	N	Y	N	N	N	19.48	140	90	76	99	10.3	4.9	93	16
129	1033379	RS	63	M	N	Y	N	N	N	31.25	130	80	73	95	15.1	8.7	107	35
130	1035215	RB	64	M	N	Y	Y	N	Y	18.22	130	100	78	99	11.8	4.9	203	40
131	1037813	GL	78	M	N	Y	N	Y	N	24.91	120	80	80	100	13.7	67	92	15
132	1071295	GS	67	M	N	Y	Y	N	Y	27.68	140	100	82	95	11	8.7	271	38
133	1078864	TR	60	M	N	Y	N	N	Y	22.11	150	90	78	98	13.4	6.8	85	29
134	1079758	SS	59	M	N	Y	N	N	Y	19.98	130	80	76	98	13.5	4.9	94	18
135	1080824	KB	75	M	N	Y	N	N	N	18.32	130	80	72	96	13.7	7.8	88	37
136	1087061	DK	56	M	N	Y	N	N	N	22.01	140	90	74	99	15.1	7.9	79	19
137	1109114	DS	60	M	N	Y	Y	Y	N	19.81	140	80	80	98	14.4	4.9	118	28
138	1110674	CP	44	M	N	Y	Y	Y	Y	22.13	140	100	68	99	9.5	5.7	277	27
139	1112201	SK	60	F	N	Y	N	N	N	19.8	120	70	80	96	11.8	8.9	94	37
140	1114336	SU	68	F	N	Y	Y	N	N	18.42	130	80	82	100	12.7	4.8	175	19
141	1121247	AK	56	M	N	Y	N	N	N	18.44	130	80	80	98	11.2	5.6	88	29
142	1121286	MS	68	M	N	Y	Y	Y	N	31.2	150	90	76	100	11.5	10	218	38
143	1121767	PK	62	F	N	Y	Y	N	N	22.1	130	100	84	99	10	5.2	278	15
144	1125450	SM	64	F	N	Y	Y	N	N	22.2	140	80	72	99	11.4	8.5	91	34
145	1178830	CS	60	M	N	Y	Y	N	N	22.12	140	80	72	98	13.5	8.7	167	26
146	1219453	PK	46	F	N	Y	Y	N	N	19.95	140	100	74	99	9.8	9.4	194	28
147	1224257	AK	69	F	N	Y	N	N	N	18.44	120	70	76	100	13.9	6.2	97	19
148	1225285	HS	64	M	N	Y	N	Y	N	20.17	130	80	73	100	12.7	8.1	86	34
149	1225628	NS	68	M	N	Y	Y	Y	N	24.11	150	90	78	98	15.8	6.3	118	32
150	1227842	KG	61	F	N	Y	N	N	Y	20.2	150	90	80	97	15.4	8.9	93	29

S No.	MRD No.	Creatinine (mg/dl)	Sodium (mmol/l)	Potassium (mmol/l)	Albumin (g/dl)	Total Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	BNP (pg/ml)	Proteinuria (Y/N)	Glycosuria (Y/N)	Echo EF (in %)	Diastolic failure in DST Echo (Y/N)
121	1019158	0.15	138	4.16	4.2	95	179	36	62	68	N	Y	60	N
122	1020407	0.48	135	3.49	3.7	294	195	49	164	95	N	N	60	N
123	1020440	0.69	139	3.67	3.6	267	179	59	130	72	N	N	60	N
124	1023014	1.01	141	3.49	3.8	210	137	47	141	84	N	Y	55	N
125	1024244	0.97	142	3.79	3.8	110	271	35	60	79	N	N	60	N
126	1025634	0.48	136	3.89	3.9	179	219	39	84	96	N	N	60	N
127	1028453	0.61	140	4.59	3.1	195	179	37	94	183	Y	N	60	N
128	1033230	0.78	145	4.15	3	179	199	49	79	97	N	N	60	N
129	1033379	0.89	134	4.26	4.2	137	120	48	62	160	N	N	60	N
130	1035215	0.15	139	4.36	2.7	271	190	47	130	79	Y	N	60	N
131	1037813	0.56	136	3.56	3.9	219	230	29	89	61	N	N	60	N
132	1071295	0.48	144	3.89	3.2	179	224	49	121	80	Y	N	60	N
133	1078864	1.08	138	3.47	3.9	199	180	28	76	167	N	N	60	N
134	1079758	0.15	139	3.59	3.8	179	198	35	68	79	N	N	55	N
135	1080824	0.48	137	3.19	3.8	197	214	48	69	98	N	N	60	N
136	1087061	0.69	145	3.46	3.7	168	130	49	59	83	N	N	60	N
137	1109114	0.27	144	3.95	3.5	179	146	27	71	120	N	Y	60	N
138	1110674	0.91	144	3.49	3.3	189	165	58	76	190	Y	N	60	Y
139	1112201	0.65	139	4.59	3.8	167	134	58	74	170	N	N	60	N
140	1114336	0.49	142	4.12	3.9	149	149	57	60	88	N	N	60	N
141	1121247	1.04	137	4.36	4.1	261	138	59	140	95	N	N	60	N
142	1121286	0.63	141	3.65	3.6	249	213	28	118	168	N	Y	60	N
143	1121767	0.45	138	3.89	2.6	220	130	32	189	192	Y	Y	60	Y
144	1125450	0.6	137	3.79	3.8	137	191	33	60	180	N	Y	60	N
145	1178830	0.94	140	3.97	3.7	179	180	49	64	145	N	Y	60	N
146	1219453	0.74	146	4.56	3.3	164	231	29	110	165	Y	N	60	N
147	1224257	0.59	139	4.12	3.5	197	180	28	79	173	N	N	60	N
148	1225285	0.65	138	4.13	3.6	189	190	49	92	134	N	N	60	N
149	1225628	0.48	141	4.02	3.9	167	170	35	91	99	N	N	60	N
150	1227842	0.61	137	4.01	3.3	291	161	32	120	62	N	N	55	N

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No. BFUHS/2K21p-TH/ 5018 Date 20/1/2021

The Principal,
DMC,Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Karanpreet Singh**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Diastolic stress test echocardiography in patients with suspected heart failure with preserved ejection fraction

Supervisor
Dr. Vikas Garg
Prof.,
Dept. of Medicine,
DMCH, Ludhiana.

Co-Supervisor
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Assoc. Prof.,
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DMCH, Ludhiana.

Dr. Abhishek Goyal
Assoc. Prof.,
Dept. of Cardiology,

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

In

MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2019

Dr. KARANPREET SINGH

DEPARTMENT OF MEDICINE
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	Diastolic stress test echocardiography in patients with suspected heart failure with preserved ejection fraction
For the degree of	M.D. Medicine
Name of the candidate	Dr. Karanpreet Singh
Supervisor	Dr. Vikas Garg Professor, Department of Medicine, DMC&H, Ludhiana
Co-supervisor	Dr. Bhupinder Singh Associate Professor, Department of Cardiology, DMC&H, Ludhiana Dr. Abhishek Goyal Associate Professor, Department of Cardiology, DMC&H, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
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Introduction: Heart failure with preserved ejection fraction (HFpEF) accounts for approximately 50% of HF cases and its prevelance relative to HF with reduced EF is rising.[1] Diastolic stress test echocardiography can offer higher sensitivity over echocardiography at rest for diagnosis of HFpEF in early stages.

Aim: The aim of the thesis is to find out the importance of diastolic stress test echocardiography in diagnosing cases of HFpEF in early stages, when BNP and echocardiography at rest are normal.

Methods and materials: A hospital based observational study involving 150 cases in OPDs of DMCH and HDHI, 75 of which are cases of suspected HFpEF and 75 cases of asymptomatic hypertension. Diastolic stress test echocardiography will be done on the same day on OPD basis to determine the proportion of cases which develop overt HFpEF during diastolic stress test.

Clinical significance: The prevalence of HFpEF is increasing. Diastolic stress test echocardiography can help in the diagnosis of HFpEF in early stages so that intervention can be done early in the course of the disease to decrease the progress of the disease.

Keywords: Echocardiography, diastolic stress test, BNP.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled "**DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION**" exist in the Department of Medicine, Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate himself/herself under our supervision and guidance.

Supervisor

Dr. Vikas Garg
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Co-Supervisor

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Associate Professor
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Associate Professor
Department of Cardiology
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Head of the Department

Dr. Dinesh Gupta
Professor & Head
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Place: _____

Date: _____

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Karanpreet Singh
Department	Medicine
Topic of Thesis	Diastolic stress test echocardiography in patients with suspected heart failure with preserved ejection fraction
Likely date of appearing in PG examination	June 2022
Date of enrollment	18th MAY,2019
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Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
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Dr. Sandeep Kaushal (Assistant Dean Academics)	Dr. Deepinder K Chhina (Professor & Head, Microbiology)
Dr. Rajoo Singh Chhina (Dean Academics)	Dr. Neena Sood (Professor & Head, Pathology)
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	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital
3	COURSE OF STUDY AND SUBJECT	M.D. MEDICINE
4	DATE OF ADMISSION OF COURSE	18th MAY,2019
5	TITLE OF THE TOPIC	Diastolic stress test echocardiography in patients with suspected heart failure with preserved ejection fraction

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Heart failure with preserved ejection fraction (HFpEF) accounts for approximately 50% of HF cases and its prevelance relative to HF with reduced EF is rising[1]. Hypertension in particular is a strong risk factor; 80 to 90 percent of the patients of HFpEF are hypertensive[2]. The diagnosis of heart failure with preserved ejection fraction (HFpEF) remains on the basis of echocardiographic analyses at rest. However, some patients with HFpEF have symptoms such as dyspnea only during exercise. Accordingly, non-invasive echocardiographic analyses at rest could be insufficiently sensitive to identify these patients. In line, recent studies demonstrated that in some patients with HFpEF left ventricular diastolic abnormalities occur only during exercise.[3] Heart failure with preserved ejection fraction (HFpEF) is an emerging global health problem of which there is limited awareness.[4] HFpEF has a prognosis similar to that of heart failure with reduced ejection fraction (HFrEF) and accounts for approximately half of all patients with heart failure.[4] Risk factors include older age, female sex, obesity, hypertension, tobacco use, diabetes mellitus, coronary artery disease (CAD), valvular heart disease and atrial fibrillation.[5] With the increase of incidence of non-communicable diseases such as diabetes mellitus, hypertension, obesity and with changing lifestyles, the incidence of HFpEF is increasing. There is a need to diagnose HFpEF at an early stage so that aggressive intervention can be pursued as early in the course of the disease as possible.

Standard 2-D echocardiography is insufficient in diagnosing cases of HFpEF in early stages as such patients develop symptoms only during stress. There is a need for better understanding of diastolic stress test echocardiography and the advantages it offers in diagnosing early cases of HFpEF, where standard echocardiography at rest has very low sensitivity.

Early in the course of the disease, a patient will have normal echocardiographic findings at rest and will have BNP with normal

range. This is the reason why HFpEF goes undiagnosed in most cases until further down the course of the disease when the patient develops symptoms at rest. In view of rising incidence of HFpEF and a very limited number of studies done on diastolic stress test echocardiography in suspected cases of HFpEF, more exploration in this field is needed so that cases of HFpEF can be detected at an early stage and early intervention can be started in order to stop or decrease the progression of the disease.

6.2 REVIEW OF LITERATURE

Heart failure with preserved ejection fraction (HFpEF), also referred to as diastolic heart failure, is characterized by signs and symptoms of heart failure and a left ventricular ejection fraction (LVEF) greater than 50%.[5] Diastolic heart failure currently accounts for more than 50% of all heart failure patients.[6] The pathogenesis of diastolic dysfunction involves abnormalities of active ventricular relaxation and passive ventricular compliance, which lead to ventricular stiffness and higher diastolic pressures. These pressures are transmitted through atrial and pulmonary venous systems, reducing lung compliance. A combination of decreased lung compliance and cardiac output leads to symptoms.[5]

A diagnosis of primary diastolic heart failure requires three obligatory conditions to be simultaneously satisfied: (1) presence of signs or symptoms of congestive heart failure; (2) presence of normal or only mildly abnormal left ventricular systolic function; (3) evidence of abnormal left ventricular relaxation, filling, diastolic distensibility or diastolic stiffness.[7]

A patient of suspected HFpEF is defined as having left ventricular ejection fraction >=50%, exertional dyspnoea, septal E/e' at rest 9–14, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) at rest <220 pg/mL[8]. HFpEF during stress is defined as E/e'>14 and LAVi>34ml/m^2.

Assessment of LV function during exercise seems to be intuitive in HFNEF patients as their symptoms occur mainly with exertion. Patients with HFNEF have limitations in increasing their LV stroke work to meet the metabolic demand at exercise due to dynamic impairment of LV active relaxation and contraction. An increase of LVFP with exertion is needed to maintain adequate LV filling and stroke volume. Recent studies have shown a variety of abnormalities of systolic and diastolic function on exercise in patients with HFNEF: reduced myocardial systolic strain, reduced ventricular systolic apical rotation at rest (which fails to increase normally on exercise), reduced mitral annular motion in systole and diastole and delayed ventricular untwisting associated with reduced LV suction.[9]

Heart failure with preserved ejection fraction typically evolves from a combination of risk factors and comorbidities, including advanced age, female sex, obesity, systemic arterial hypertension, diabetes mellitus, renal dysfunction, anaemia, iron deficiency, sleep disorders, and chronic obstructive pulmonary disease.[10]

Chronic hypertension is the most common cause of diastolic dysfunction and failure. It leads to left ventricular hypertrophy and increased connective tissue content, both of which decrease cardiac compliance. The hypertrophied ventricle has a steeper diastolic pressure-volume relationship; therefore, a small increase in left ventricular end-diastolic volume (which can occur with exercise, for example) causes a marked increase in left ventricular end diastolic pressure.[11]

Most measures that use E/e' to characterize LV function are obtained at rest. While overt LV diastolic and systolic dysfunction can be readily identified by conventional diagnostic techniques including echocardiography, the initial stages of myocardial dysfunction may be hidden by compensatory mechanisms, especially at rest. In patients with a similar grade of DD at rest, there can be a spectrum of alterations in diastolic function during exercise.[12]

The evaluation of left ventricular diastolic function at rest is an integral part of echocardiography. If first degree of diastolic dysfunction is found in the resting examination, or if there is a large clinical suspicion of heart failure and the previous examination does not give us the final diagnosis, it is worth to refer the patient to the echocardiographic diastolic stress test.[13]

Traditional models of HFpEF pathophysiology revolve around systemic HTN and other causes of increased left ventricular afterload leading to left ventricular hypertrophy (LVH) and diastolic dysfunction. However, emerging models attribute the development of HFpEF to systemic proinflammatory changes secondary to common comorbidities which include HTN. Alterations in passive ventricular stiffness, ventricular-arterial coupling, peripheral microvascular function, systolic reserve, and chronotropic response occur.[14]

The central paradigm involves a systemic proinflammatory state triggering a downstream cascade of cardiac microvascular endothelial activation, oxidative stress, and abnormal myocardial cyclic guanosine monophosphate signaling, leading to microvascular rarefaction, chronic ischemia, fibrosis and progression to HFpEF.[15]

N-Terminal pro-B type natriuretic peptide levels were below the level considered to exclude disease (<=125 pg/mL) in 18% of subjects with HFpEF. E/e' ratio was correlated with directly measured pulmonary capillary wedge pressure at rest (r=0.63, P<0.0001) and during exercise (r=0.57, P<0.0001). Although specific, current guidelines were poorly sensitive, identifying only 34% to 60% of subjects with invasively proven HFpEF on the basis of resting echocardiographic data alone. Addition of exercise echocardiographic data (E/e' ratio>14) improved sensitivity (to 90%) and thus negative predictive value, but decreased specificity (71%).[16]

Intense research has implicated multiple factors in the etiology of HFpEF syndrome including systemic inflammation, LV hypertrophy, slowed LV relaxation, increased LV stiffness and remodeling, increased peripheral vascular resistance, impaired endothelial dysfunction, increased pulmonary vascular resistance, and neurohormonal activation. Ventricular-arterial coupling has been suggested as a more unifying theory. When arterial circulation becomes "stiffer," the afterload increase is responsible for elevated blood pressure and progressive loss of LV elasticity with higher filling pressures. Groups more prone to develop HFpEF include those with obesity, diabetes, hypertension, and chronic kidney disease.[17]

Stroke volume and its change during exercise should be also assessed. In

fact, unlike in a normal compliant heart, there is no increase in left ventricular end-diastolic volume during exercise and consequently no increase in cardiac output in heart failure with preserved ejection fraction. The absence of increased cardiac output during exercise is, like E/e' and estimated pulmonary artery pressure, a major parameter to be investigated during submaximal exercise performed to confirm

the diagnosis of heart failure with preserved ejection fraction as an etiology of dyspnea.[18]

All imaging techniques can provide an ejection fraction, but the versatility of echocardiography makes it unique in the provision of volumes, diastolic function, right ventricular function, hemodynamics, and valvular regurgitation. The early detection of heart failure has been facilitated by the assessment of global longitudinal strain, which is also useful in later heart failure for the assessment of left ventricular synchrony. The use of echocardiography has been associated with favorable outcomes, probably on the basis of facilitation of appropriate therapy.[19]

Echocardiography remains an essential procedure in HF. Echocardiography allows for accurate diagnosis and prognosis in both HFrEF and also in HFpEF. Future research should focus on combining echocardiographic prognostic markers into easily applicable prediction models in order to aid clinical decision making.[20]

Recent publications suggest that diastolic dysfunction is the primary cause of heart failure in 30-50% of patients. Several studies also show that, in a significant number of patients with systolic dysfunction, diastolic function is the major determinant of their symptomatic status, their response to treatment and their outcome. Other preliminary data suggest that diastolic dysfunction is an important cause of exercise intolerance in patients with chronic hypertension.[21]

Plasma BNP levels were lower and associated with predominantly LV concentric remodeling/hypertrophy, presumably derived from age-related higher systolic and pulse pressures or aortic stiffness in the HFpEF patients than in the HFrEF patients, who were associated predominantly with eccentric hypertrophy. The results imply that LV concentric remodeling/hypertrophy and hence less end diastolic wall stress stimulates less BNP production in HFpEF as compared with HFrEF. These findings strongly suggest that the pathogenesis and hence management of HFpEF may be distinct from those of HFrEF.[22]

Patients with suspected HFpEF (left ventricular ejection fraction 50%, exertional dyspnoea, septal E/e' at rest 9–14, and N-terminal pro-B-

type natriuretic peptide (NT-proBNP) at rest 220 pg/mL; n = 13) and a control group constituted from asymptomatic patients with arterial hypertension (n = 19) and healthy subjects (n = 18) were included. All patients were analysed by two-dimensional and Doppler echocardiography at rest and during exercise (DST) and underwent cardiopulmonary exercise testing and NT-proBNP analysis during exercise. HFpEF during exercise was defined as exertional dyspnoea and peak VO2 20.0 mL/min/kg. In patients with suspected HFpEF at rest, 84.6% of these patients developed HFpEF during exercise, whereas in the group of asymptomatic patients with hypertension and healthy subjects, the rate of developed HFpEF during exercise was 0%. Regarding the diagnostic performance of DST to detect HFpEF during exercise, an E/e' ratio >15 during exercise was the most accurate parameter to detect HFpEF (accuracy 86%), albeit a low sensitivity (45.5%). Nonetheless, combining E/e' with tricuspid regurgitation (TR) velocity 2.8 m/s during exercise provided a significant increase in the sensitivity to detect patients with HFpEF during exercise (sensitivity 72.7%, specificity 79.5%, and accuracy 78%). Consistent with these findings, an increase of E/e' was significantly linked to worse peak

VO2, and the combination of an increase of both E/e' and TR velocity was associated with elevated NT-proBNP values during exercise.[8]

6.3 AIMS AND OBJECTIVES OF THE STUDY

The purpose of this study is to assess the potential usefulness of DST echocardiography in diagnosing patients with HFpEF in early stages by analyzing DST findings in patients with suspected HFpEF and asymptomatic patients with arterial hypertension.

7. MATERIALS AND METHODS

A hospital based observational study of 150 patients from OPDs of DMC and HDHI. The patients will be divided into 2 groups. The first group will contain patients with suspected HFpEF which is defined as having left ventricular ejection fraction >=50%, exertional dyspnoea, septal E/e' at rest 9–14, TRV<2.8m/s, E/A<1, LAVi<=34ml/m^2 and BNP at rest 50-200 pg/mL.[8][13]. The second group will contain asymptomatic patients with hypertension. Each group will contain 75 cases each. The results obtained will be studied as to the proportion of patients in each group to develop overt HFpEF during stress, which is defined as E/e'>14, TRV>=2.8m/s, E/A>=1 and LAVi>34ml/m^2.[13]

7.1 Source of Data

A hospital based observational study will be conducted at OPD of Dayanand Medical College and Hospital and Hero DMC Heart Institute, Ludhiana which will include 150 cases as described. It will also include a written proforma which will include epidemiological information such as age, sex, occupation and place of residence, present history of complaints and past history of similar complaints and comorbidities, general and systemic examination, diagnosis, routine investigations, BNP levels and resting and stress echocargiographic findings.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

- Age 18 years and above
- Willing to give consent for the study

EXCLUSION CRITERIA:

- Age less than 18 years
- Cardiac arrhythmias or pericardial diseases
- Abnormal 2-D echocardiography study
- CKD or CLD
- Structural heart diseases like cardiomyopathies and valvular heart defects
- Prior coronary intervention
- Anemia with Hb less than 8 g/dl
- Respiratory diseases like COPD

•Not willing to give consent for the study

•Coronary Artery Disease

DURATION OF STUDY – 18 months.

SAMPLE SIZE – 150 cases.

METHODOLDGY – 150 cases of suspected HFpEF will be studied. The following parameters will be considered:

- Hb:
- TLC:
- DLC:
- RBS:
- RFT:
- LFT:
- LIPID PROFILE:
- BNP:
- URINE ROUTINE:
- 2-D ECHO:
- DIASTOLIC STRESS ECHO:

The findings will be studied and the proportion of cases which develop HFpEF during diastolic stress test echocardiography in each group will be analyzed.

OUTCOME- To evaluate the usefulness of diastolic stress test echocardiography in diagnosing early cases of HFpEF by evaluating patients with suspected HFpEF and asymptomatic cases with hypertension, and studying the proportion of cases in each group to convert to overt HFpEF during stress test echocardiography.

STATISTICAL ANALYSIS- Continuous data will be presented as mean ± standard deviation and dichotomous data in percentage. Differences in continuous variables between groups will be analyzed using Student's t-test. Categorical variables will be compared by chi-square test and Fisher's exact test as appropriate. Comparisons between three or more groups will be analyzed using a one-way analysis of variance. Differences will be considered statistically significant when $P<0.05$.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

2D ECHOCARDIOGRAPHY, DIASTOLIC STRESS ECHO

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

8. LIST OF REFERENCES

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PROFORMA

1. NAME
2. MRD No
3. AGE
4. GENDER
5. ADDRESS

6. MOBILE No
7. CHIEF COMPLAINTS
   - DYSPNEA ON EXERTION
   - CHEST PAIN
   - PALPITATIONS
8. HISTORY OF PRESENTING ILLNESS
   - DYSPNEA ON EXERTION
     - ONSET
     - PROGRESSION
     - DURATION
     - NYHA GRADE
   - ORTHOPNEA
   - PND
   - CHEST PAIN
   - PALPITATIONS
9. CO-MORBIDITIES AND PAST HISTORY--
   - HYPERTENSION
     - DURATION
     - JNC GRADE

Signature of Candidate **Signature of Supervisor**

- DIABETES MELLITUS
    - DURATION
    - BLOOD SUGAR CONTROL
- PERIPHERAL VASCULAR DISEASE
- STROKE OR TIA
- HYPERCHOLESTEROLEMIA

10. PERSONAL HISTORY
    - ALCOHOL INTAKE
        - DURATION
        - AMOUNT
    - SMOKING
        - DURATION
        - AMOUNT
    - OBESITY
        - BMI (kg/m^2)
        - WHO CLASSIFICATION GRADE
11. DRUG HISTORY

12. GENERAL EXAMINATION—
    - HEIGHT (m)
    - WEIGHT (kg)
    - BMI (kg/m^2)
    - PALLOR
    - CYANOSIS

Signature of Candidate **Signature of Supervisor**

- ICTERUS
- ANKLE EDEMA
- PERIORBITAL EDEMA
- JVP
- VITALS:
    - BP (mm)
    - HR (/min)
    - RR (/min)
    - SpO2 (%)

13. SYSTEMIC EXAMINATION

- CVS
    - APEX BEAT
        - PALPABLE
        - LOCATION
        - TYPE
    - S1
    - S2
    - S3
    - S4
    - MURMUR
        - LOCATION
        - TYPE
        - RADIATION
        - GRADE
    - RADIORADIAL DELAY

Signature of Candidate **Signature of Supervisor**

- RADIOFEMORAL DELAY

- GIT
  - ABDOMINAL DISTENSION
  - DISTENDED VEINS
- RESPIRATORY
  - AIR ENTRY
  - BREATH SOUND
  - VESICULAR OR BRONCHIAL BREATHING
  - FINE CREPTS
  - COARSE CREPTS
  - RHONCHI

14. DIAGNOSIS

15. ROUTINE INVESTIGATIONS

- Hb (g/dl):
- TLC (/mm^3):
- DLC:
  - NEUTROPHILS (/mm^3):
  - MONOCYTES (/mm^3):
  - LYMPHOCYTES (/mm^3):
  - EOSINOPHILS (/mm^3):

Signature of Candidate **Signature of Supervisor**

- BASOPHILS (/mm^3):

- RBS (mg/dl):
- RFT:
  - UREA (mg/dl)
  - CREATININE (mg/dl)
  - SODIUM (mmol/l)
  - POTASSIUM (mmol/l)
  - CHLORIDE (mmol/l)
- LFT:
  - SGOT (U/L)
  - SGPT (U/L)
  - ALP (U/L)
  - TOTAL BILIRUBIN (mg/dl)
  - DIRECT BILIRUBIN (mg/dl)
  - ALBUMIN (g/dl)
  - TOTAL PROTEIN (g/dl)
- LIPID PROFILE:
  - TOTAL CHOLESTEROL (mg/dl)
  - TG (mg/dl)
  - HDL (mg/dl)
  - LDL (mg/dl)
- BNP (pg/ml):
- URINE ROUTINE:
  - PROTEINURIA (+/-)
  - GLUCOSURIA (+/-)

Signature of Candidate **Signature of Supervisor**

- CHEST X-RAY:
  - PLEURAL EFFUSION
  - CARDIOMEGALY
  - KERLEY B LINES
  - INTERSTITIAL EDEMA
- ECG:
  - RATE (/min)
  - SINUS RHYTHM
  - AXIS (degree)
  - P WAVE
    - TYPE
    - DURATION (sec)
  - PR INTERVAL (sec)
  - QRS COMPLEX
    - TYPE
    - DURATION (sec)
  - ST ELEVATION
  - ST DEPRESSION
  - QT INTERVAL (sec)
  - LVH CHANGES
  - RVH CHANGES
  - HEART BLOCK
    - DEGREE
  - PREMATURE VENTRICULAR CONTRACTION
  - INTRAVENTRICULAR CONDUCTION DEFECT

Signature of Candidate **Signature of Supervisor**

16. 2-D ECHO:

- AORTIC ROOT (mm):
- LEFT ATRIUM (mm):
- RIGHT ATRIUM (mm):
- RVID (D) (mm):
- IVST (D) (mm):
- IVST (S) (mm):
- LVID (D) (mm):
- LVID (S) (mm):
- LVPW (D) (mm):
- LVPW (S) (mm):
- EF (%):
- END DIASTOLIC VOLUME (ml):
- END SYSTOLIC VOLUME (ml):
- VELOCITY GRADIENT:
  - MV (cm/sec):
  - AV (cm/sec):
  - TV (cm/sec):
  - PV (cm/sec):
- MURMUR GRADE:
  - MR:
  - AR:
  - TR:

Signature of Candidate **Signature of Supervisor**

- PR:

- E/e':
- TRV (m/sec):
- LAVi (ml/m^2):
- E/A:
- IMPRESSION:

17. DIASTOLIC STRESS TEST ECHO:

- AORTIC ROOT (mm):
- LEFT ATRIUM (mm):
- RIGHT ATRIUM (mm):
- RVID (D) (mm):
- IVST (D) (mm):
- IVST (S) (mm):
- LVID (D) (mm):
- LVID (S) (mm):
- LVPW (D) (mm):
- LVPW (S) (mm):
- EF (%):
- END DIASTOLIC VOLUME (ml):
- END SYSTOLIC VOLUME (ml):

Signature of Candidate **Signature of Supervisor**

- VELOCITY GRADIENT:
  - MV (cm/sec):
  - AV (cm/sec):
  - TV (cm/sec):
  - PV (cm/sec):
- MURMUR GRADE:
  - MR:
  - AR:
  - TR:
  - PR:
- E/e':
- TRV (m/sec):
- LAVi (ml/m^2):
- E/A:
- IMPRESSION:

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....

.....am willing to participate in the study **"DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION."** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **'DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"DIASTOLIC STRESS TEST ECHOCARDIOGRAPHY IN PATIENTS WITH SUSPECTED HEART FAILURE WITH PRESERVED EJECTION FRACTION" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ